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ANOXIA RESULTING FROM METHANE

REPORT OF CASE

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In view of the fact that the majority of homes in the metropolitan area of New Orleans are heated with open, radiant, gas burning heaters, it is not surprising that anoxia resulting from natural gas poisoning occurs frequently. These heaters are potentially hazardous for several reasons: Drafts of air may extinguish the flame; defective plumbing may permit leaks; the jets may become completely or partially plugged with dirt, rust or corrosion; and there is a propensity for many inhabitants to permit the flame to burn while they sleep. The natural gas utilized in the homes and industries of New Orleans consists chiefly of methane, not carbon monoxide as many believe. The purpose of this paper, therefore, is to acquaint physicians of this community with the above facts and to summarize the pharmacologic effects of methane and of the anoxia resulting therefrom, together with a case report to illustrate the management of these cases.

An analysis of the natural gas distributed in New Orleans is as follows:

Carbon dioxide (CO_2)	0.40
Oxygen (O_2)	0.00
Ethane (C_2H_6)	4.62
Methane (CH_4)	94.23
Nitrogen (N_2)	0.75
	100.00 per cent

Specific gravity 0.604
Btu (Sat. 30" Hg. & 60° F.)

It will be seen from this analysis that the natural gas of this community does not contain any carbon monoxide. However, improper adjustments in open gas heaters may lead very readily to the production of carbon monoxide, and natural gas poisoning in this area may be the result of methane poisoning, carbon monoxide poisoning, or both, depending upon the lack of, or the conditions of, combustion. Both methane and carbon monoxide are asphyxiants, substances which induce a deficiency in the supply of oxygen to the tissues through some means other than interference with the mechanics of respiration[1]. Such substances produce their action solely by interference with oxygenation. Carbon monoxide is a chemical asphyxiant and combines with hemoglobin, thereby excluding oxygen. Methane is a simple asphyxiant producing its effects only by exclusion of oxygen. As Henderson and Haggard have pointed out, the effect of methane as an asphyxiant is proportional to the extent to which it diminishes the partial pressure of oxygen.

Methane is produced whenever organic matter decomposes. It is one of the gases found in the intestine. Cellulose decomposes to form methane, carbon dioxide and volatile fatty acids. There is no evidence

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that methane may be further decomposed in the human body. Wells, quoted by McGuigan,[2] reported a case of pneumothorax in which the products of decomposition by putrefactive saprophytes contained 4.3 per cent hydrogen, 6.25 per cent methane, and traces of hydrogen sulfide. In nature, methane is the principal constituent of "fire damp" and serves as a cause of explosions in coal mines, whereas the term "after damp" is applied to the gaseous mixture remaining in mines after the explosion. Most physiologists agree that the physiologic effects of "after damp" result from either an excess of carbon monoxide or a deficiency of oxygen.

The volatile hydrocarbons when inhaled produce depression of the central nervous system. Some, such as ethylene, cyclopropane and acetylene, are effective general anesthetic agents; methane, ethane, and other saturated hydrocarbons are not suitable for this purpose. According to Adriani,[3] methane was first utilized as an anesthetic agent in 1867. In a review of gaseous anesthetics in 1924, W. E. Brown[4] found methane to have a very narrow zone of safety, unconsciousness occurring when the alveolar air reached 87 per cent by volume and death by asphyxia at 90 per cent. In view of the 94 per cent mixture of methane in the natural gas of this area, asphyxiation can readily result from excess inhalation of natural gas. According to McGuigan, Herter found that a mixture of 79 per cent methane and 21 per cent oxygen can be inhaled without effect. Luessum,[2] on the other hand, noted that inhalation of 80 per cent methane and 20 per cent oxygen for twenty minutes produced slight anesthesia with ringing in the ears, redness of the face, and dizziness. The pulse was unaffected. Recovery occurred in a few minutes. Obviously the hazard of explosion is an additional disadvantage to the use of methane as an anesthetic agent.

CASE REPORT

M. L., a 34 year old, white male, was admitted to the accident room of Charity Hospital at 11:10 p. m., January 10, 1944, in a state of unconsciousness and marked dyspnea. A history gathered from friends disclosed that he had been ill with an upper respiratory infection and that he had remained in his room with the doors and windows closed for twelve or more hours with the radiant heater burning. The flame had been extinguished by unknown factors while he was sleeping. The patient had a suffused appearance, Cheyne-Stokes respirations at a rapid rate, and the pupils were equal and reacted to light. His blood pressure was 115/80, pulse 110, rectal temperature 102° F. There were no rales in his chest or other evidences of pulmonary edema. The most significant feature of the physical examination was the marked respiratory distress during which he breathed deeply and rapidly with periods of marked hyperventilation alternating with periods of hypoventilation. These periods were separated by two minute intervals. During the period of hyperventilation, it was noted that marked carpopedal spasm and hypertonicity of all muscles were present. He was treated with oxygen by nasal catheter, repeated pharyngeal aspiration, calcium gluconate intravenously, a transfusion of 500 c.c. of whole blood, an infusion of 1,000 c.c. of saline, 100 c.c of M/6 sodium lactate, and 200 c.c. of Ringer's lactate in 5 per cent glucose, one ampule (2 c.c.) of metrazol intravenously, and 0.3 gm. of phenobarbital administered in three hourly dosages of 0.1 gm. each to control muscular activity. Observations of pulse, respirations, temperature, blood pressure and general condition were recorded at fifteen minute intervals for the next seven hours. No significant changes were noted but it was felt that it would be safe to transfer him to the ward.

His course in the hospital for the ensuing week was stormy. His temperature rose to 105.5° F. (rectal) on the following day and both physical and roentgenographic evidences of bronchopneumonia were present. Sodium sulfadiazine was administered by the intravenous route. His temperature gradually returned to normal by the end of the first week of illness. Coma continued for four days then gradually improved for the next three days. Cheyne-Stokes respirations, as previously described, were observed for two full days before improvement occurred. Weakness of the left side of the face was noted and intermittent muscular spasms were present. On January 12, two days after the asphyxiation occurred, all members of the staff concurred in a grave prognosis. The attending neurologist elicited bilateral Babinski and Hoffman's reflexes and absent abdominal reflexes. It was his impression that the patient had scattered cerebral injury which caused both the fever of 105° F. and the deep coma.

Therapy at that time consisted principally of symptomatic and supportive measures. Oxygen by nasal catheter, temperature measures of alcohol sponges, intravenous sodium sulfadiazine, intravenous medications to maintain both nutrition and fluid, and nursing care were the chief agents. Nine hours later, the patient began to improve clin-

ically and gradual recovery ensued during the next several days. The depth of the coma passed gradually to lucidity; respirations and temperature returned to normal; the patient began to recognize attendants; later he could eat; and all neurologic manifestations subsided except for partial deafness in both ears which persisted until he was discharged.

The laboratory data are of interest in that hemograms, urinalyses, blood cultures, spinal fluid surveys, and periodic blood chemical determinations for blood glucose, carbon dioxide combining power, serum chloride, and blood urea nitrogen were consistently within normal limits except for a mild acidosis (carbon dioxide combining power of 30 per cent) on admission, which gradually returned to normal levels during the next 36 hours. A spectroscopic examination of the blood failed to reveal any evidence of carbon monoxide. When bronchopneumonia developed, a leukocyte count of 31,600 was noted and the differential count revealed 86 per cent polymorphonuclear cells. An electrocardiogram made on January 13 revealed a low auricular or junctional pacemaker and low T-waves which were interpreted as being toxic in type. On January 19, the electrocardiogram was normal.

On January 28, 1944, when he was discharged, the patient was completely well except for slight impairment of hearing. No neurologic residuals could be demonstrated by physical examination and an electroencephalogram made on January 26, two days prior to discharge, was interpreted as manifesting normal rhythm.

COMMENT

Two mechanisms, asphyxia and narcosis from the inhaled methane, were doubtless operative in the clinical picture presented by this patient. Of the two, that of asphyxia or cerebral anoxia seems to be the more important, although it should be emphasized that the effects of anoxia in the production of surgical anesthesia are still incompletely evaluated. Courville[5] has presented an exhaustive review of this subject and has outlined the clinical course and sequelae of asphyxia. Apparently the state of asphyxia was prolonged and severe, conditions under which definite central nervous system degeneration occurs. Prolonged sublethal asphyxia alone may be responsible for these changes and in the present patient is accountable for the symptomatology seen as well as the sequel of impaired hearing. The fact that this patient left the hospital with impaired hearing may be interpreted as cerebral damage of a more or less permanent character and agrees well with the cases studied by Courville. The patient also showed pulmonary sequelae initially, the result of atelectasis and leading to bronchopneumonia. Methane has no direct irritant action upon the respiratory tract[1].

Treatment of methane poisoning is, in the acute stages, removal from the source and institution of oxygen therapy, preferably combined with 5 to 7 per cent carbon dioxide. Such therapy will, if the exposure has been of short duration, effect relief of symptoms in a few hours. Added therapeutic agents are necessary in prolonged asphyxia, as brought out in the present case. These measures are symptomatic and supportive. Headache, for example, may persist in the postasphyxial period from edema of the cerebral tissues and demand dehydration by administration of hypertonic solutions or spinal tap for relief. Pulmonary edema and pneumonia give rise to appropriate measures to combat these states. Great variation in the therapeutic procedures will arise depending on the indications in the specific case.

SUMMARY

A case of anoxia following methane inhalation (natural gas poisoning) in New Orleans exemplifying the problems in therapy and the occurrence of sequelae, has been presented.

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MISSED LABOR*

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Missed labor is the term applied to a fetus that dies *in utero*, is retained there for

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months, undergoing mummification or putrefaction, according to whether or not the membranes have ruptured.

Menzies and Hennig record two cases, one being retained for two hundred and eighty and the other two hundred and ten days respectively, after full term. In the former instance it was removed at autopsy; in the latter, after incision of the cervix. Flatau records an extraordinary case in which the condition persisted for fifteen years, when the fetal bones were removed from the uterus at autopsy.

The etiology of the condition is not known. In the cases reported by Labhardt it was associated with carcinoma of the cervix and myoma of the uterus. Ciulla is inclined to associate the phenomena with excessive fatty degeneration of the uterine musculature.

The symptomatology varies from a few painful uterine contractions with a cessation of fetal movements to those of weakness, lassitude, the development of secondary anemia, waxy appearance, and fever. The physical findings are those associated with a dead fetus.

The treatment should be induction of labor as soon as the diagnosis is made. If induction by the usual methods fails, then more drastic steps have to be taken; this depending on the condition of the patient.

CASE REPORT

Mrs. L. A. B., white female, aged 31, a housewife, was first seen on July 22, 1943. Her chief complaints were nausea, vomiting, pains in the upper right abdomen referable to the right shoulder for the past two weeks. She had noted a mass in the lower abdomen. The menstrual history had been regular every 28 days, lasting two days, associated with severe cramps. Her last normal period was April 10, 1943. She has had three pregnancies, the first of which ended in a living baby now six years old; the second in an ectopic pregnancy for which she was operated on; and the third in a criminal abortion in May, 1942. Examination revealed an enlarged uterus to the size of a five months' pregnancy.

Progress: On August 19, 1943, fetal movements were felt. During the next three months pregnancy developed normally; fetal heart tones were heard and the height of the fundus increased. The only untoward complaint during this interval was "spotting", associated with cramps. Progesterone was given at this time in an effort to stop these findings. An x-ray taken at this time revealed a fetus about seven months.

On December 29, 1943, fetal movements stopped; heart tones were no longer heard; the height of the fundus, which has reached 28½ cm., began diminishing.

On January 6, 1944, a Freidman-Lapham test was reported negative.

On January 20, 1944, the patient was hospitalized for induction of labor. Medical induction with pituitrin and pitocin failed to incite labor, and an attempt to introduce catheters was made. The cervix was found firm and scarred and could not be dilated more than enough to pass a 14-F catheter. It was hoped that even this would act as a stimulation to uterine contractions and cause sufficient dilatation to introduce a Voorhies bag. An x-ray taken after this procedure showed a dead fetus of approximately seven months with a rubber catheter lying to the right and posterior to the fetus. The head of the fetus was well up in the uterine cavity. On failure of this procedure to induce labor, consultation was asked for. The consultant expressed the opinion that the patient probably had a premature separation of the placenta (this having caused the fetal death) and that since the methods used had failed to incite labor, and the patient's condition being good, that she be allowed to go home; that if bleeding returned or the patient showed any toxic manifestation, that she be admitted for a Porro section. She was discharged from the hospital on January 1, 1944.

For several weeks after returning home her general condition remained good except for the development of a secondary anemia. For this she was given liver extract intramuscularly. She was also given large doses of an estrogenic substance (10,000 units daily of thelestrin for 10 days) with the hope of inciting labor pains. With reasonable waiting and with the patient's condition becoming toxic, she was re-hospitalized on March 8, 1944, for operative intervention.

Under general anesthesia the patient's abdomen was opened after excising an old midline scar. The uterus was the size of an eight months' pregnancy. An incision was made transversely at the vesicouterine reflection, the bladder reflected downwards and the serosa of the uterus upwards. The uterus was then opened longitudinally. On entering the amniotic sac, a sero-sanguineous, slightly pungent fluid was drained. A male, shriveled-up fetus was extracted without difficulty. An effort to exteriorize the uterus was met with difficulty. Further exploration showed the uterus to have a thin, friable wall that did not contract with pituitrin injected directly into its musculature, and bowel and omentum were adherent to it on all sides. Exploration of the uterine cavity showed that the placenta was implanted firmly over the internal os and that attempt to free it caused

bleeding. Since the uterus could not be freed sufficiently (without greatly jeopardizing the patient's life) for the performance of a hysterectomy, the following alternate procedure was instituted: The cord was transfixed with chromic No. 1 close to the placenta and the excess cord removed; the bladder peritoneum and serosa of the uterus were sutured to the parietal peritoneum; the uterine musculature was sutured to the fascia. This was done for the full extent of the uterine incision. The skin and fascia above and below this area were closed in the usual manner. The uterine cavity was packed with lap sixes, two in number.

The patient postoperatively ran fever to 101.6° for two days, returning to normal on the third day. She received blood and fluids parentally during the first 24 hours. She made an uneventful recovery, leaving the hospital on the eleventh postoperative day. The initial lap sixes were removed in 36 hours and the wound re-packed. The entire placenta had sloughed out by the time she had left the hospital.

The uterine wound took four months to close completely, each month discharging menstrual blood. She has menstruated normally since then.

SUMMARY

This case report is presented to you because of its unusual features:

1. The infrequency of the condition.
2. Failure to go into labor with the usual methods of induction. This may have been due to the firm, scarred cervix and a soft, flabby uterine wall which was incapable of being stimulated.
3. The necessity for surgical intervention.
4. The interesting operative findings—placenta previa centralis; the soft, friable uterine wall; the marked omento-intestinal adhesions.
5. The operative procedure employed to handle the findings.

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DISCUSSION

Dr. Vincente D'Ingianni (New Orleans): I saw this patient recently; menstruating normally, per vagina, the abdominal incision was completely closed. After viewing the pathology about the uterus, it was thought that the patient should be permitted to recover and return at a later date; for exploration, possibly hysterectomy. However, after a year or more this woman has no complaints, menstruating normally and is having a normal sexual life. This case points out the fact that when nature is given a chance to recover it often does so; therefore we must not be too hasty in doing extensive surgery.

Dr. E. L. Zander: I saw this patient in consultation and I want to call attention to the members that this procedure is rather an unusual operation. In reviewing cases at Charity Hospital from 1935 to 1945 we found one case reported out of the various operated on for ruptured uteri with pregnancy. Dr. Graffagnino performed a section at that time and did the same procedure as was followed in this particular case. I recommend a Porro because there have been many Porros performed at Charity Hospital for this type of case. I thought it the method of choice rather than vaginal section. The surgeon accepted that view, and, would have met with trouble if he had attempted a vaginal section. As it was he found no lesions and I think he is to be commended because the results speak for themselves. It is certainly something that should be called to our attention and should be remembered in this type of case and I think conservatism in some cases is to be recommended rather than radical procedures which we resort to in complicated cases.

I think the surgeons presented a splendid case. There are lots of unusual features about it; especially when the case did not go into labor with any procedure attempted and in the long run the results were one hundred per cent. I think both surgeons are to be complimented.

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REVERSIBLE HEART DISEASE

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In general when one speaks of heart disease the immediate thought is of an invalid or at least a person in so-called "delicate health" who will be forced to spend the rest of his life on a more or less subdued scale and who may or may not live to a ripe old age depending upon the severity of the process and the intelligence of the physician and patient. Recently, as our knowledge has progressed there have come to be recognized certain forms of heart disease in which the prognosis is much better than in the usual types and indeed permanent cures may be effected by proper methods of treatment. Such forms of heart disease may be termed "curable" or reversible heart disease. Although relatively rarer than the

more serious diseases of the heart, their importance to both the patient and the physician is easily recognized.

According to Eppinger and Burwell[2] "the word cure is used to indicate: (1) the inactivation or abolition of a disease process while its effects are still reversible, and (2) the repair of a disabling mechanical defect left by some injury or disease no longer active." Accordingly, they classify patients with curable heart disease into three groups as follows: "(1) A group of patients in whom the cardiac disability is the result of severe mechanical overload of the heart. The lesions or defects leading to such overload include patent ductus arteriosus, arteriovenous fistula, thyrotoxicosis and possibly anemia. (2) A group of patients in whom the cardiac disability results from a mechanical obstruction to the entrance of blood into the heart. Such obstruction occurs in the various forms of cardiac tamponade, notably those due to constrictive pericarditis, suppurative pericarditis and acute hemopericardium. (3) A group of patients in whom the cardiac disability is due not to a gross mechanical abnormality, but to a dysfunction of the cardiac muscle. This group includes patients who suffer from beriberi heart and the so-called myxedema heart."

Not included in this classification are such conditions as are produced by pregnancy, infectious diseases such as diphtheria, syphilis in the early stages, hypertension due to the Goldblatt kidney, and those due to neurogenic disorders. These are only mentioned in this paper for the sake of completeness, since they are relatively rare conditions as compared to the other forms of reversible heart disease which will be discussed. Syphilis, while by no means rare, is still not considered by many authors to cause heart disease that is reversible in the sense that the others to be discussed are. However, there have been many studies to show that cardiovascular syphilis can be prevented by prompt and early treatment.[5, 11]

THYROTOXIC HEART DISEASE

As Levine[11] has stated "This subject is probably the most important aspect of all heart disease for it comprises the one large group of cases in which the difference between accurate and inaccurate diagnosis and treatment is the difference between chronic invalidism or death and restoration of life and health."

We are all familiar with the cardinal symptoms and signs of thyrotoxicosis such as exophthalmos, nervousness, loss of weight with increased appetite, palpitation, fine nervous tremor and enlargement of the thyroid gland and in a patient who presents these symptoms the development of dyspnea, palpitation, chest pain, cough, edema of the feet and ankles, would at once be suspected as being caused by the thyroid condition and proper therapy employed. It is in that group of so-called "masked thyrotoxics" that these latter symptoms and signs may not be properly understood. Then the patient may be diagnosed as having some form of heart disease, usually mitral stenosis, because of the presence of a rough apical systolic or diastolic murmur or both, with a snapping first sound, or he may be diagnosed as having hypertensive heart disease. Levine and Sturgis[13] noted in 1924 that these cardiac symptoms may be the only ones of developing hyperthyroidism for a number of years. A patient may even develop congestive failure without presenting signs or symptoms to make the unwary aware of the true nature of his trouble.

The mechanism by which this thyrotoxic heart is brought about is not definitely understood but it is thought to be due to the increased load on the heart due to the increase in basal metabolism and also possibly to some direct action of thyroxin upon the cardiac musculature.[18] There is an increase in blood volume, peripheral vascular dilatation, and accelerated blood flow, all of which increase the work of the heart. "This burden is not discontinuous, like that of physical exertion, but is present both day and night."[2]

The majority of these patients are over 40, but Levine and Likoff, in a review of 409 cases of thyrotoxicosis submitted to subtotal thyroidectomy between 1923 and 1941, found six instances of congestive fail-

ure in patients under the age of 41 and three under the age of 30 when there was absolutely no evidence of other lesions such as rheumatic valvular disease, hypertension, or coronary artery disease. Of this group of patients 331, or 81 per cent, showed no other type of heart disease.[15] As we know, hyperthyroidism occurs four or five times more frequently in the female than in the male and therefore we would expect cardiac manifestation to follow a similar incidence and this seems to be the general consensus.

The symptoms and signs such a patient presents on visiting the physician may be varied. Levine and Sturgis[13] report five cases in which the chief complaint was palpitation, pain or dyspnea of over two years' duration. Eppinger and Burwell[2] report a case in which the mistaken diagnosis of mitral stenosis versus hypertensive heart disease was entertained for a considerable period of time. The patient had nothing referable to the thyroid gland until it was noted that he perspired much more profusely than would be suspected in a patient on complete bed rest. A basal metabolism was run and found to be elevated and under iodine therapy the patient showed marked improvement. Subtotal thyroidectomy was performed with excellent results.

In general the chief signs and symptoms of a patient with this form of heart disease will be: dyspnea, cough, edema, palpitation, chest pain and perhaps congestive failure. Attacks of paroxysmal auricular fibrillation occur frequently and Hurxthal considers this as important in hyperthyroid heart disease as glycosuria in diabetes. Some patients present a typical and severe anginal syndrome and this is the basis for performing thyroidectomy in such cases. However, operation primarily for the relief of the anginal pain is not favored at the present, as the benefits do not justify the operative risks or medical complications arising from the induced hypothyroidism. Geiger[6] reports only one apparent cure of the anginal syndrome in a series of five patients undergoing operation.

Diarrhea, weakness and nervousness, loss of weight, and increased sweating may be suggestive symptoms and of course those other symptoms mentioned above as being characteristic of hyperthyroidism are of importance. Irregular heart rate with tachycardia, large pulse pressure, edema, slight elevation of the systolic blood pressure, enlargement of the heart and extrasystoles may occur. A sign which Carter[20] considers pathognomonic, if arteriosclerosis and aortic insufficiency can be ruled out, is the pistol-shot sound heard in the cubital fossa. When cardiac dilatation takes place an apical systolic murmur may develop and the heart sounds may become snappy and forceful in character with an abrupt forceful apex beat. The basal metabolic rate will be elevated and when this condition is suspected an electrocardiogram should always be made to confirm the diagnosis. Electrocardiographic changes are not particularly characteristic and may show only sinus tachycardia or later evidence of congestive heart failure. The fluoroscope, according to Sosman,[18] may be of great value in suspecting this condition. The heart under the fluoroscope shows not only a rapid rate but "a vigorous, snappy hyperactive beat, in many cases just the reverse of what would be expected with a given degree of heart failure or anginal pain".[18] It is of interest that such hyperactivity may be seen in other forms of curable heart disease, such as beriberi heart, severe anemia, arteriovenous fistula, patent ductus arteriosus, as well as in neurocirculatory asthenia and pneumothorax.

Of particular importance is the fact that patients with severe symptoms of heart disease or failure, fail to show the expected response to the usual modes of treatment, such as complete bed rest, digitalization and diuretics. Such an occurrence should at once make us suspect this condition. The circulation time is usually normal or more rapid and this is an unusual feature of the condition.

The prognosis in this type of heart disease, when once recognized, is very good and under proper treatment a large majority of these patients can expect a complete

reversal of their condition with a return to a useful and pleasant life. According to Levine, the prognosis and mortality rate in these patients who are older than the usual thyrotoxic patient are as good or better than in the younger patients with exophthalmos.

The treatment of this condition is the same as that for other forms of hyperthyroidism, that is, subtotal thyroidectomy with preoperative use of iodine. In many cases the response to iodine therapy may be so good that the patient will refuse operation but it must be remembered that eventually the patient will become refractory to the use of iodine. The use of quinidine preoperatively, if the patient is in auricular fibrillation, is a controversial matter. The Lahey group in Boston does not use it preoperatively, since most patients recover spontaneously after the thyroid is removed; if not, then quinidine is administered. The group at Massachusetts General Hospital uses quinidine preoperatively except in those patients with active auricular fibrillation beginning 24 hours before operation and continuing 24-36 hours following the operation. As in those patients with the usual hyperthyroid state, rest and sedation are of importance to allay their fears and worries. Following operation most of these patients show a rapid and remarkable improvement.

CHRONIC CONSTRICTIVE PERICARDITIS

This is a condition which has been frequently overlooked and which has not been well understood until recent years. Claude S. Beck[1] has studied the condition from both the experimental and clinical viewpoint and some of his conclusions are of interest. The heart in this condition is small and quiet. It functions efficiently as far as the valvular and muscular mechanics are concerned but its action is still inadequate, due to the fact that less blood can get into the heart because of the compression. Beck is of the opinion that the heart muscle can actually undergo atrophy of disuse as a result of the decrease in the work load. He does not believe that adhesions *per se* are of any importance clinically in causing the symptoms and signs of congestive heart failure.

There are two types of compression of the heart, the acute and the chronic. The acute type is brought on by such things as a penetrating wound of the heart, or the rapid accumulation of pus in pericardial cavity, rupture of a myocardial infarct or hemorrhage from a myocardial contusion. The chronic type may be produced by slow hemorrhage, or accumulation of pus in the pericardial cavity, mediastinal effusion, infections such as rheumatic fever followed by formation of scar tissue, with contracture or chronic effusions due either to pyogenic organisms or tuberculosis. Tumors may also cause a chronic compression.

The mechanism by which the two conditions are brought about varies and thus gives rise to two triads which are helpful in their diagnosis. In the acute compressions the triad consists of "(1) a small quiet heart, (2) a rising venous pressure, and (3) a falling arterial pressure." That for chronic compression of the heart consists of "(1) a small quiet heart, (2) a high venous pressure, and (3) ascites and enlargement of the liver." In the chronic type other signs and symptoms which are the result of increased venous pressure such as engorgement of the veins of the head and neck, enlargement of the liver, ascites, fluid in the pleural cavity or edema, are present. Electrocardiographic changes are not characteristic for either condition. The x-ray is often of value in confirming the diagnosis. Under the fluoroscope the heart will show diminished or absent pulsations. It may be enlarged only slightly, if at all. If there are adhesions to the diaphragm it may show an abnormal jerk with each systole. With the passage of time calcified plaques become visible which can be demonstrated in the x-ray or by fluoroscopy. A tachycardia or rapid beating of the heart may be visible under the fluoroscope.[18] In addition to the above the findings of normal N.P.N. and blood sugar levels, blood counts and urine, with a normal or only slightly lowered serum protein level, and normal liver functions tests in a patient showing

symptoms and signs as above, should make us suspect the condition.[6]

Treatment of these conditions is surgical and very good results are reported by most workers.[1, 5, 6, 11] In the acute compressions, aspiration of the pericardium or open operation may be life-saving measures. In the chronic cases pericardectomy is frequently followed by complete and permanent recovery. In those cases which do not show the rapid recovery that one would expect Beck[1] believes that atrophy of disuse in the heart muscle is to blame. We may conclude, however, that this condition also belongs in the realm of reversible or curable heart disease.

PATENT DUCTUS ARTERIOSUS

This condition which formerly carried with it a very serious prognosis is now considered in properly selected cases to be a form of reversible heart disease. This is brought about through the field of surgery. Gross,[8] in 1939, reported on the first successful case of a patent ductus which was closed by surgical ligation in 1938. Since that time he has reported on a total of ten cases, eight of which were definitely improved. Of the other two, one died from a *Staphylococcus aureus* infection and the other proved to have another associated cardiac abnormality.[8] Others have reported similar results.

The condition is not as rare as one might think and it is estimated by Keys and Shapiro that at least 20,000 persons in the United States have a patent ductus arteriosus at the present time. Although there are cases reported of such persons living a normal life expectancy, in the majority of cases death ensues before 30 years of age. Death is usually due to either sudden or slow cardiac failure or to a subacute bacterial endocarditis.

The condition may also cause physical underdevelopment or invalidism in a growing child. It may not manifest itself at birth, not being recognized in some cases until the fourth year of life.

The diagnosis of the condition is comparatively easy. There is usually a loud, characteristic "machinery murmur" that may be heard over the entire precordium, in the axilla and back loudest in the third interspace to the left of the sternum. The patient may show retardation of growth and shortness of breath.[17] A thrill may be felt over the pulmonic area. The heart may be enlarged to percussion and other physical findings, but will almost always show some enlargement on x-ray. The diastolic blood pressure is significantly low, while the systolic may show no change. Since the blood is flowing from the arterial to the venous side of the circulation the patient will not show cyanosis unless there is some complicating lesion to cause it. The electrocardiogram is not characteristic and may show either left or right axis deviation, usually the former. X-ray studies have been carried out by Eppinger and Burwell[3] and by Sosman[81] and the changes seen are thought to be of valuable aid in establishing the diagnosis although not diagnostic in themselves. These consist of:

"1. The heart is usually enlarged, especially the left ventricle.

"2. The pulmonic artery (often incorrectly called the 'pulmonary conus' is more prominent than normal, projecting anteriorly and to the patient's left.

"3. The hilar vessels are enlarged, due to engorgement, especially on the right side, where they are normally larger and more easily visible.

"4. In less than half of the cases systolic pulsation of the hilar vessels can be seen fluoroscopically, the so-called 'hilar-dance.'

"5. The left auricle has been dilated posteriorly in nearly all of our cases, so much so in some patients as to make me believe there was an associated mitral stenosis, later proved incorrect.

"6. There is a striking hyperactivity of the left ventricle and an associated increased expansile pulsation of the dilated pulmonary artery synchronous with the hyperactive ventricular systole. Both decrease strikingly after ligation of the ductus".[18]

These findings in addition to those of the physical examination make the diagnosis of patent ductus arteriosus comparatively easy.

It is important that studies be made to rule out associated cardiac abnormalities which would render the effects of surgery negligible. Leaman[11] states that in patients living until the seventh year there is little chance of there being an associated defect.

Operation is carried out only in a selected group of patients. Those showing underdevelopment, cardiac decompensation or failure are probably definitely justifiable indications. As a preventive measure against the development of subacute bacterial endocarditis it is probably not indicated as strongly, although a few cases with excellent results have been reported following operation.

Treatment, as mentioned above, consists of surgical ligation of the patent ductus, and in the usual case the patient shows immediate and marked improvement.

ARTERIOVENOUS ANEURYSMS

This condition is somewhat similar to that of a patent ductus arteriosus except that in this condition both circulatory systems are involved with an increased blood flow present in both the systemic and pulmonary circulation. The condition may produce eventual heart failure that may occur even months or years after the opening of the fistula. This fistula may also be the site of an endarteritis caused by *Streptococcus viridans* with consequent septicemia and embolic phenomena.[5, 11]

The arteriovenous communication may be either congenital or acquired, the latter usually resulting from trauma such as a gun-shot wound in the femoral or popliteal regions. The patient will usually suffer from edema of the involved extremity and intermittent claudication and ischemic neuritis. Over the fistula one can palpate a thrill and pulsation while the skin shows increased heat. A murmur may be heard over this area. As the result of the increased flow of blood with increased venous return the heart is overworked to the point of hypertrophy and congestive heart failure in some cases. "Cardiovascular findings closely resemble those found in aortic regurgitation, beriberi heart and thyrotoxicosis."[17]

Treatment of this condition results in surgical ligation or removal and there usually is a marked improvement in the patient's condition. Indeed, cures have been reported in those cases in which the aneurysm contained vegetations of *Streptococcus viridans* and Leaman[11] reports a case which he believes would have resulted in cure had the patient received treatment at an earlier date.

ANEMIA AS A CAUSE OF REVERSIBLE HEART DISEASE

A decrease of hemoglobin below 50 per cent is known to produce a necessary increase in the work of the heart as a result of the relative anoxemia. On the other hand, a severly anemic patient, as in pernicious anemia, may show signs and symptoms of congestive heart failure as a result of the underlying anemia. Hookworm infestations are a frequent cause of such severe anemias.

These patients present themselves with dyspnea, fatigability, weakness, precordial pain, the hemic murmurs, and an enlarged and dilated heart which may have progressed to the stage of congestive heart failure. Circulation time may be more rapid or normal; the blood pressure low and an increase in cardiac output and oxygen utilization. X-ray shows a hyperactive heart which is usually enlarged. [5, 18]

The diagnosis in these patients is based upon the blood picture and demonstrations of the underlying cause. Therapy consists of transfusions, liver, iron, rest in bed and supportive therapy. Digitalis and diuretics are of value in some cases of congestive failure, more so in this condition than in some of the other forms of heart disease discussed in this paper.

THE MYXEDEMA HEART

This constitutes probably the most controversial subject of all those considered in the scope of his paper. Zondek, in 1918, described the "myxedema heart" as follows:

I. Before treatment with thyroid.

"1. Dilatation of the left and right heart which may be of a very high degree.

"2. Slow, indolent heart action with

normal blood pressure.

"3. Lowering of the aricular wave and the T-wave of the electrocardiogram.

"II. Following treatment with thyroid.

"1. Return of the heart from marked dilatation to somewhere near normal size.

"2. More lively heart action and more rapid pulse without change in the blood pressure.

"3. Gradual return of the P and T waves to normal."[12]

Fahr in this country has described a condition similar to that described by Zondek and agrees with him that there is a condition characterized as above which is properly termed the "myxedema heart". Fahr[1] reports a number of cases which bear out his theory that congestive heart failure is frequently seen in myxedema and that these conditions will clear up rapidly following thyroid therapy and that they will show little, of any, improvement under the usual therapy used for congestive heart failure.

Other workers from their studies of myxedematous patients have definitely disagreed with Zondek and Fahr and state that they found no such condition as that described by them and that any myxedematous patients having heart disease had some cause for it other than the myxedema. Criticism has been directed toward this group however because their cases have not been as carefully followed with x-ray and other studies as have those of the proponents of the myxedematous heart.

It seems that a more or less middle of the road attitude is the best to take in considering this condition. As stated by Means, White and Krantz[16] the results of their studies with those of others would "seem to justify the conclusion that 'myxedema heart' in the sense of Zondek and of Fahr, is far from common. On the other hand, we are not prepared to join those who feel that it does not exist." Lerman, Clark and Means[12] agree with these workers and are of the opinion "that the heart in myxedema is usually enlarged and decreases in size when thyroid is administered and that the change in the size of the heart is of diagnostic importance." They differ from Fahr as shown by the following statements. "Cardiac failure due to myxedema is uncommon and slight if present. It is practically always associated with hypertension and arteriosclerosis."

The cause of the increase in heart size in myxedema is not well understood. Experimentally cretinoid sheep and goats have shown evidence at autopsy of cardiac dilatation and a flabby myocardium, and it is generally considered that there is a loss of muscle tonus and an interstitial edema which occurs in the hearts of some myxedematous patients similar to conditions found in the other parts of the body.

The electrocardiographic changes, that is, inversions of the T waves, lowering of the P waves and QRS complexes or negative QRS complexes, have been shown to occur not only in the myxedema heart of Zondek and Fahr, but are also found in other myxedema patients as well and thus cannot be considered as strictly characteristic. However, these will also show changes toward the normal under thyroid therapy.

The blood pressure has also been observed to be somewhat elevated in these cases of myxedema[12] while others[4] have reported cases with no change in the blood pressure. However, in those cases with an increased blood pressure there was usually a tendency to return to normal following thyroid therapy. Those cases showing the least improvement were those with associated hypertension or arteriosclerosis. It is also of interest that those patients showing hypertension and arteriosclerosis more clearly fit the term "myxedema heart" as used by Zondek and Fahr, that is, cardiac dilatation with congestive heart failure than those patients who do not have the conditions. However, it has long been known that myxedema predisposes to arteriosclerosis.

Other findings may be present such as peripheral edema, rales in the lung bases, enlargement of the liver, which may be considered as due to the heart condition, but it should be remembered that they

might be caused by the underlying disease primarily. Of course in these cases the usual symptoms and signs of myxedema, such as dry, scaly skin, mental dulness, puffy eyelids, or diminished basal metabolic rate, are present.

In summary it seems that the following conclusions may be drawn. There is a condition which occurs in some patients with myxedema which is characterized chiefly by enlargement of the heart, electrocardiographic changes, and changes in the blood pressure which may, though usually do not progress to congestive heart failure. Such a condition does not respond in the usual manner to digitalis and the routine therapy which is used, but will respond, in some cases markedly, to the use of thyroid extract, and therefore can be considered as being due primarily to the myxedematous condition.

In regard to therapy with thyroid extract it is wise to remember that too rapid use may cause coronary occlusion or anginal attacks. The former is thought to be due to the associated coronary sclerosis that is seen with a decrease in the size of the lumen of the coronary vessels at the same time that the work of the heart is increased by the raising of the metabolic rate. The latter condition may be brought about in a similar manner. In a patient who begins to show anginal pain under thyroid therapy it is probably best to regulate the therapy so that a middle path is followed increasing the metabolic rate as much as possible and yet stopping short of the point which will produce anginal symptoms.

HEART DISEASE DUE TO VITAMIN DEFICIENCY

Beriberi, which may be defined as "a complex clinical syndrome which follows failure to ingest, absorb or utilize sufficient amounts of vitamin B_1, is the only deficiency state which in the light of our present knowledge is associated with definite circulatory disturbances and failure."[18]

This type of deficiency syndrome with its effects upon the heart and circulation has long been known in the Orient. Wenckebach and Aslsmeer who studied the condition in Java reported from their case histories and autopsy findings a typical syndrome and popularized the term "beriberi heart." Race, age, sex, diet, country and other factors tend to change this typical picture when it is studied by other workers. Weiss and Wilkins[19] found in Boston many patients who were evidently suffering circulatory disturbances and/or cardiac failure but who presented wide variations from the typical Oriental beriberi of Wenckebach.

There are essentially two types of beriberi, the "dry" in which the signs are chiefly referable to the nervous system and the "wet" in which there is edema of varying degree and with which type circulatory disturbances are mainly manifest. Combinations of the symptoms and signs of these two types are of course possible but my discussion will be limited for the most part of the "wet" type and in this form nervous symptoms are liable to be minimal or absent.

The mechanism by which the beriberi heart is brought about is still not too well understood. The theory which was formerly accepted was advanced by Japanese workers who considered the cardiac disease to be due to a disturbance in function and a degeneration of the vagus nerves.[19] They based their theory on the tachycardia and evidence histologically of demyelinization of the vagus nerves. Such changes are not always seen and consequently this theory has fallen in disrepute. Wenckebach thought that there was a peculiar hydroptic degeneration in the heart muscles, that is, edema of the heart muscle due to a disturbance in water metabolism, which causes a loss in power of contractility and resistance to stretching. In addition to this there is a dilatation of the arterioles which allows an increased volume of blood to flow more rapidly to the right heart with resultant dilatation and failure of the right heart. Accordingly, Wenckebach characterized his "beriberi" heart on the findings of right sided heart failure without evidence of left heart failure which is made worse by the administration of adrenaline

and improved by the administration of pitressin.

Weiss and Wilkins[19] disagree with Wenckebach and state that the "cardiovascular disturbances caused by nutritional defects do not form a rigid clinical syndrome," and they are unable to demonstrate a significant difference in the water content of the heart in patients suffering from deficiency heart disease as compared to patients with normal hearts or who suffered from organic heart disease with anasarca. Also they have studied patients who presented evidence of left heart involvement or failure and have described electrocardiographic changes in such patients, while Wenckebach demonstrated only one type of deficiency syndrome which occurred in Java and there may be other types or, as stated above, other factors such as race, age, country, diet, or occupation, may cause a different type of response to the deficiency.

The observations of other workers when correlated together make the picture a little more complete. "The first of these is that vitamin B_1 is a catalyst necessary in complete oxidation of carbohydrate, the lack of which decreases the contractile power of heart muscle. The second is the observation of Harrison and Pilcher that edema *per se* increases the work of the heart and thus would secondarily contribute to the production of heart failure. The third is the frequent observation that subjects with beriberi who have a polyneuritis of a degree still permitting physical effort are the most likely to develop heart failure."[10] These three factors are all present in most patients with beriberi who develop congestive failure.

The Oriental form of beriberi occurs most frequently in coolies or the lower classes and seems to be directly related to a dietary deficiency, since rice constitutes the basic staple of their diet. It is known that in the process of polishing, the vitamin B content of rice is greatly diminished. In the United States, although the problem is basically a deficiency, other factors than economic may play a part in its development. According to Goldsmith[7] the average American diet is apt to be deficient in this vitamin since it contains such a large percentage of sugar and highly refined cereals from which the "B" vitamins have been removed. It is only recently that the addition of vitamins to the processed foods or development of other processing methods have been used to overcome this source of deficiency.

Alcohol probably plays a more important part in the development of dietary deficiencies in this country than perhaps any other factor and a history of alcoholism or at least "heavy drinking" can be obtained from a majority of these patients. Its role is thought to be purely secondary due to the fact that it is a "food substance *par excellence* in this part of the world, and it supplies the body with the necessary calories but with a minimum of vitamin "B", an ideal combination of factors for the development of beriberi." There is also clinical evidence "that a high carbohydrate diet in animals and a pure rice diet in man predispose to clinical vitamin B deficiencies and it is possible that alcohol, as a carbohydrate, in large amounts may act the same way."[19]

In addition, other factors, such as elevation of the body requirements for vitamin B_1, as in fever, hyperthyroidism or pregnancy, dietary fads and idiosyncrasies, gastrointestinal disturbances which prevent proper absorption or utilization of the vitamins, may play a part and should be searched for in all such cases.

The symptoms of vitamin B_1 deficiency are not necessarily characteristic although those of a peripheral neuritis usually will cause us to consider the possibility. It is in those cases in which cardiovascular symptoms are prominent with little or no evidence of nervous involvement that the diagnosis may be most frequently missed. Symptoms and signs in this group include edema, dyspnea, tachycardia, right or left ventricular failure, enlargement of the heart, gallop rhythm, systolic murmurs and a normal or decreased circulation time. X-ray evidence of a hyperactive heart beat

or pericardial effusion may be seen. The electrocardiogram shows findings, which though not necessarily characteristic or specific, add to the picture. These are shortened P-Q intervals, flattening of the T waves or low voltage and negative T_3 waves, and prolongation of the Q-T interval. In some cases acute circulatory collapse may ensue.

Of special importance in these findings is the shortened or normal circulation time and the response to digitalis therapy is not always as marked as would be expected in heart failure from the usual causes. These findings are similar to those seen in thyrotoxicosis, but the basal metabolism is usually lower in beriberi.

The diagnosis is based upon the elimination of the usual organic heart diseases, a history of alcoholism or dietary deficiency, and if the response to adequate amounts of vitamin B_1 is marked the diagnosis will be established. The nervous manifestations of the disease are also aids in diagnosis.

The prognosis in these patients, if the diagnosis is established early, is very good especially in regard to the circulatory manifestations which clear up much sooner than the nervous changes when present.

Treatment consists of adequate amounts of thiamin chloride given either parenterally or orally, plus an adequate diet. Joliffe and Rosenblum[10] suggest as much as 1000 mg. in divided doses within 24 hours in persons with marked circulatory collapse or severe congestive failure. In less severe cases they recommend the parenteral administration of 20-200 mg. thiamin chloride daily in two doses intramuscularly. Goldsmith[7] states that the therapeutic dose may vary from 5 mg. daily in a mild deficiency to 15-30 mg. daily in a severe neuritis to 50-100 mg. daily in the acute cardiac form of the disease.

The patient should be kept at absolute bed rest in failure because of the danger of death following exertion. An adequate diet should be given and vitamin B supplemented orally by means of brewers' yeast or other preparations.

The underlying cause of the defect should be looked for and eliminated.

SUMMARY

There are several diseases in which the heart is so affected that it may be considered the primary disturbance and the underlying lesion overlooked. In these cases the heart changes are frequently reversible if their cause is removed. It is of importance to both the physician and the patient that these conditions be recognized and treated early, since after a variable length of time the heart condition may pass beyond the stage of reversibility.

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THE BLOOD PRESSURE IN CORONARY OCCLUSION

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The purpose of this paper is to correlate blood pressure and the various aspects of coronary occlusion, namely: (1) etiology; (2) clinical picture; (3) its bearing on prognosis in the immediate attack; (4) its bearing on the ultimate prognosis. There is much discrepancy in the literature regarding this subject; therefore, any conclusions reached reflect the opinions of this writer and are not to be taken as the ideas of those investigators whose clinical material and statistics are cited in this paper.

In the past twenty years, there have been no more than five articles written about the blood pressure variations in myocardial infarction, and yet there are relatively few physicians who are not familiar with these changes, although the great majority are not cognizant of its implications. The scarcity of this subject in the literature has no explanation, as there have been hundreds of thousands of cases available in the large general hospitals of this country. These should have served as clinical material for much research concerning the role played by the blood pressure in the factors which are discussed in the present writing.

ETIOLOGY

Hypertension is a common antecedent of coronary occlusion and was concluded by Levine to be the most significant single etiologic factor, since it occurred in at least 40 per cent of his patients. Others have reported the incidence of hypertension to be from 25 to 75 per cent.

TABLE 1
INCIDENCE OF KNOWN HYPERTENSION IN PATIENTS WITH CORONARY OCCLUSION

Authors	Criteria	Cases of Coronary Occlusion	Cases of Hypertension	Incident Per cent
Barnes and Ball	S. 150 D. 100	42	24	57
Boas and Donner	S. 150	57	....	25
Connor and Holt	.....	274	93	35
Cowan and Ritchie	S. 150	58	28	48
Eschbach	.....	50	....	75
Levine	S. 150 D. 100	148	58	40
White and Bland	S. 160 D. 110	200	50	25
Palmer and McGill	S. 160 D. 100	212	155	73
Master	S. 150 D. 90	800	499	62

S=Systolic D=Diastolic

Allen,[1] in 1934, in a study of the incidence of hypertension in patients with coronary occlusion, as compared to the incidence of hypertension in the general population, found that there is definitely a higher proportion in the former group. Frost and Knight state that hypertension was present in 2 per cent of more than 600,000 candidates for life insurance. Janeway states that in a large group of unselected patients, the incidence of hypertension was 11 per cent. This latter figure was based on a systolic blood pressure of 165 mm. of mercury or more. Although there is no way of arriving at the true incidence of hypertension in the general population, it can be seen from the above figures that there is a far greater incidence in those individuals having attacks of coronary occlusion than there is in the population as a whole.

TABLE 2
INCIDENCE OF HYPERTENSION IN THE GENERAL POPULATION

Authors	Criteria	Cases	Per cent
Janeway	S. 165	.....	11.0
Mayo Clinic	S. 160	3377	7.9
Frost and Knight	.....	600,000	2.0

Master, Dack and Jaffee[12] have concluded that as a result of their statistical analysis of more than 800 cases of coronary occlusion, hypertension is an etiologic factor in coronary occlusion, for its incidence is definitely greater than that calculated for the general population. Furthermore they state that the unit attack ratio per hypertensive male was five to eight times greater than that for patients with normal blood pressure, although both ratios increased with age in the same proportion.

If we are to accept the fact that hypertension is an etiologic factor, there must be some explanation for the discrepancy that exists between the incidence of coronary occlusion in the two sexes.

The male sex is more often affected by coronary heart disease than is the female. The ratio of coronary occlusion in female and males is about one to four. The ratio

of hypertension in females and males is about three to two. If hypertension is an etiologic factor *per se*, these figures must be explained.

TABLE 3
CORONARY OCCLUSION INCIDENCE IN THE TWO SEXES

Author	Cases	Male	Female
White and Jones	.....	60%	40%
White and Bland	461	85%	15%
Parkinson and Bedford	83	72%	11%
Clawson	1215	82%	18%
Glendy, Levin and White	100	96%	4%

I have attempted to find some basis for the assumption that hypertension is an etiologic factor. I have reached the conclusion that there are only two means by which hypertension can produce coronary occlusion. The first is purely theoretical while some basis exists for the presence of the second.

(1). Hypertension of long standing is responsible for ventricular hypertrophy. This probably will serve to place greater demand on the coronary blood supply and at the same time cause a reduction in the calibre of the smaller arteries as a result of pressure from the neighboring hypertrophied myocardium. This process may proceed to the point where only the hypostatic pressure within the vessel will prevent the external pressure from causing a complete occlusion. A partial occlusion would exist and a condition would be present where as a result of decreased hydrostatic pressure (such as would occur in spinal anesthesia) the external pressure on the vessel being exerted by the myocardium could completely occlude the vessel and infarction would occur. This would be an example of coronary occlusion without thrombosis.

(2). The basic pathology upon which the vast majority of the cases of coronary occlusion occur is the presence of atheroma in the coronary arteries. Many investigators postulate that hypertension is a cause of atherosclerosis, and if this is true it will explain the means whereby hypertension serves as an etiologic agent.

Atheroma is a softening and a precursor of arteriosclerosis, with yellowish fatty areas in the endarterium. Fibrosis, thickening, and calcification ensue and the arteries become brittle. Hemorrhage from the rupture of minute vessels in the vascularized atherosclerotic walls of the diseased coronary arteries is thought by some to favor or precipitate coronary thrombosis.

Garfield Duncan[26] states that in the general population the sclerosis of the coronary arteries is five times more common in men than in women. Vander Veer observed that in the last 100 cases of infarction of the myocardium which resulted from coronary occlusion at the Pennsylvania Hospital, there were 81 men and 19 women, giving a ratio of four to one. Other investigators have arrived at approximately the same resulting ratio. This tends to show a definite correlation between the incidence of atherosclerosis and coronary occlusion.

Although hypertension and arteriosclerosis are frequently associated it is unlikely that the latter is the cause of the former. It is more plausible that prolonged hypertension is a factor in the sclerosis of arteries. It is known that with prolonged elevation of the blood pressure, sclerotic changes in the retinal vessels will become apparent.

The true cause of atheroma of the coronary arteries has not yet been discovered. Faulty cholesterol metabolism, local arterial strain, overwork of the heart and vascular system, hypertension, infection, allergy, endocrinopathy, and heredity are all possible factors but none of them have been proved causes. The incidence of association of hypertension and atherosclerosis has no real correlation as there is an inverse relationship between the two conditions in the two sexes, although there is in general an association.

I believe that prolonged hypertension with subsequent enlargement of the heart may possibly be a factor in the production of coronary occlusion, but the manner in which it is responsible is not known. Until this is discovered it cannot be stated that hypertension is a definite factor in the etiology of coronary occlusion.

BLOOD PRESSURE IN THE CLINICAL PICTURE

In a typical attack of coronary occlusion there is an initial rise in blood pressure. This transitory increase in blood pressure is rarely over 30 mm. of mercury systolic

and is practically never over 60 mm. of mercury. The severe pain which occurs at the onset of the attack is believed to be responsible for this initial rise. Unless the patient is observed by the physician in the first hour or two following the occlusion, this transient rise is not detected as the blood pressure will have reversed and assumed a lower level. It is this drop in blood pressure that is characteristic of myocardial infarction.

The low blood pressure varying from 75 to 100 mm. of mercury systolic and 50 to 75 diastolic may continue for days, tending gradually to resume the former level that existed before the occlusion or a somewhat lower level. The explanation for the blood pressure drop is stated by Paul White[25a] to be the combined results of vasodilation, myocardial weakness, and bed rest. This explanation is certainly logical as any one of these factors is capable of lowering the blood pressure, and we must concede that all three are present in an attack of coronary occlusion.

Master, Dack, and Jaffee[10] analyzed the blood pressure changes in 538 cases of coronary occlusion in 1943. Their findings were not significant as they correlated with the clinical picture discribed in most writings on the subject, but the series serves as a basis upon which the conclusions as to the probable incidence and degree of blood pressure changes are present in any given number of cases.

In this series of 538 cases, the blood pressure fell to some extent in every case. A rapid fall was observed to be more common than a gradual drop in the pressure. Occasionally the fall did not occur until a week following the occlusion. In some cases it was observed that the initial fall was soon followed by a temporary or a permanent rise in the blood pressure. These investigators also found that the trend of the pressure was similar in the hypertensive and non-hypertensive groups, although they found that a rapid fall was more common among the non-hypertensive patients who died during an acute attack.

The systolic blood pressure rarely falls below 90 mm. of mercury in the hypertensive group but in the non-hypertensive group it is very common for the systolic pressure to go below this level. When the blood pressure falls below a systolic pressure of 80, the patient usually dies.

It is interesting to note that in Master's series 20 per cent of the patients with a previous pressure exceeding 200 mm. of mercury systolic did not have a fall below 150 mm. of mercury.

IMMEDIATE PROGNOSIS

The size of the infarct is directly responsible for the amount of drop in blood pressure. It has been proved experimentally in animals that the larger the infarcted area, the greater the decrease in cardiac output, therefore the greater the drop in blood pressure. White [25a] has observed that in patients having small and medium sized infarcts, the blood pressure is only slightly reduced; and this reduction is believed by him to be the result of bed rest.

Hoskin[4] has concluded as a result of analysis of coronary occlusion in private practice that a systolic blood pressure below 90 is an indication of a serious myocardial damage and a pressure below 80 practically always signifies a high mortality. Still many cases with a systolic pressure of 80 recover, but if the pressure continues to remain low the prognosis is very poor, and according to Hoskin the survival period is under two years in this event.

Levine [24b] states that in his cases, he has observed that a systolic pressure which was around 170 mm. of mercury before the attack, drops to about 110 mm. although this change takes places over a period of several days. Master's series in 1943 showed about the same degree of drop in pressure. In those individuals with a normal blood pressure the drop frequently reaches the low level of 80 mm. of mercury. It is in this latter group that the immediate prognosis is so bad, as the pulse pressure is greatly decreased and extreme shock is manifested. The prognosis in this group, whose pressure reaches a systolic level below 80 and a pulse pressure of 20 or less, is extremely poor.

I believe that with the same degree of

myocardial infarction in two given cases, one case having a previous hypertension and the second case having a previous normal blood pressure, there will be a proportional drop in the pressure in the two cases. The hypothetical evidence for this assumption lies in the circulatory dynamics necessary for the maintenance of blood pressure. Those factors which combine to maintain the normal blood pressure are: (a) pumping action of the heart; (b) peripheral resistance; (c) quantity of blood in the arterial system; (d) viscosity of the blood; (e) elasticity of the arterial walls.

Assuming that the last four of the above factors are not changed by the coronary occlusion and subsequent infarction, we will limit our explanation to factor number one, the pumping action of the heart.

The means by which the cardiac contraction exerts its effect upon the arterial blood pressure is through the quantity of blood which it is capable of discharging into the aorta in a unit period of time. Therefore the work of the heart depends chiefly upon the amount of blood ejected per minute against the mean pressure in the aorta. If the other factors already mentioned remain constant, the product of the pulse pressure and the heart rate may be used as an index of the energy of the pumping action of the heart.

In a hypothetical case of a patient who has a blood pressure of 180/92 the pulse pressure is 88. If the rate is 70, we have an index of $88 \times 70 = 6160$. In a second hypothetical case, the patient has a normal blood pressure of 120/80 and a pulse pressure of 40 the index is $40 \times 70 = 2800$. With myocardial infarction severe enough to reduce the ventricular contraction force by 30 per cent, there is a corresponding reduction in the minute volume. Since it is assumed that all other factors remain constant, the indices will likewise have a 30 per cent reduction. Therefore the resulting indices are 4050 and 1870, respectively. If the pulse rate increases to 100 per minute which it would do following occlusion, the pulse pressures in the two cases would be 40 and 19, respectively. Thus it can be seen that the drop in blood pressure is directly proportional to the previous standing pressure.

It has been observed by many investigators that the lower the blood pressure and pulse pressure, the greater the mortality in the acute cases. Therefore it appears to me that an antecedent hypertension offers a better prognosis than a previous normal pressure. This has not been substantiated by other writers, however. Master[12] concludes that hypertension does not affect the immediate prognosis, as the mortality rate in his series of 800 cases was about the same for hypertensive and non-hypertensive patients, in spite of a considerable increase in the incidence of cardiac enlargement in the former group. Couver and Holt, and Vander Veer and Brown also stated that they had not found any relationship between hypertension and the immediate mortality rate.

I have attempted to establish some reason why there should be no correlation between hypertension and a low mortality rate, as it has been seen that shock and death, as a result thereof, is less common in those patients with an initial hypertension. The explanation may lie in the fact that many people with coronary occlusion die of massive pulmonary edema weeks after the occlusion and these deaths are placed among those in the acute stage. The massive pulmonary edema is practically always predisposed to by the presence of a long standing hypertension.

Master has found a constant association between cardiac enlargement and heart failure. In his series[7] the heart was enlarged in 63 per cent of the patients. Evidence of cardiac insufficiency, usually of both ventricles was present in 90 per cent of the cases. Although dilatation must theoretically occur in a normal sized heart which becomes insufficient, six patients with heart failure following coronary occluson showed no clinical evidence of enlargement despite the presence of congestive failure. The incidence of enlargement in patients who developed congestive failure was 87 per cent. Only 20 per cent of

patients who did not develop insufficiency had an enlarged heart. This investigator concluded that patients with coronary occlusion are much more prone to develop congestive heart failure when cardiac enlargement is present. Thus it may be seen that hypertension can indirectly be responsible for failure, as it is the most frequent cause of cardiac enlargement.

ULTIMATE PROGNOSIS

To determine the prognosis in the individual case at the time of the attack may be most difficult. There is an impression that the prognosis depends in part on the severity of the initial manifestations and this is probably true. The size of the cardiac infarct is of great importance because the future efficiency of the heart depends on the extent of the infarct and the integrity of the remaining muscle.

The presence of hypertension following recovery from coronary occlusion certainly tends to make the future prognosis poor. I do not believe that high pressures will predispose a person to more attacks than would be expected in a non-hypertensive individual who has recovered from the first occlusion. The hypertension will probably tend to increase the work of the already damaged heart to such an extent that some insufficiency will occur. In the event of a second occlusion, there would be little reserve for the heart and a rapid congestive failure would be more likely.

Palmer[15] in 1937 charted the blood pressure reading of 61 patients who had coronary occlusion. The blood pressure, previous to the attack as well as blood pressure each year subsequent to the attack, was recorded.

In analyzing these 66 cases of coronary occlusion, I have found that among 19 deaths that occurred in the six years following the first attack, eight were due to subsequent attacks of coronary occlusion. Of the 19 deaths, 17 exhibited hypertension with a systolic pressure greater than 160 or a diastolic pressure more than 100. All eight of the patients who died of subsequent attacks of coronary occlusion had a previous hypertension. There were 22 subsequent attacks of coronary occlusion in the 66 cases, and as stated before eight deaths resulted. Of these 22 subsequent attacks nine had normal blood pressures. Only one patient with a normal blood pressure died as a result of a subsequent attack of coronary occlusion as compared to seven who had hypertension.

TABLE 4

INCIDENCE OF ATTACKS OF CORONARY OCCLUSION, HYPERTENSION, AND DEATH IN 66 PATIENTS WHO WERE FOLLOWED FOR SIX YEARS AFTER RECOVERING FROM THEIR INITIAL ATTACK OF CORONARY THROMBOSIS (FROM PALMER)

Years Following Attack	1	2	3	4	5	6	Total
Deaths	5	3	5	2	1	3	19
a) With hypertension	5	3	5	1	1	2	17
b) Due to coronary occlusion	2	2	2	1	0	1	8
Subsequent Coronary Occlusion	9	5	3	3	1	1	22
a) Deaths	2	2	2	1	0	1	8
b) With hypertension	5	2	1	0	1	0	9
Coronary Deaths	2	2	2	1	0	1	8
With Hypertension	2	2	2	1	0	1	8

In view of the evidence we are obliged to assume that hypertension definitely is a menace to life in those patients who have had a previous coronary occlusion.

SUMMARY

1. I have attempted to correlate blood pressure and coronary occlusion as to (a) etiology; (c) clinical picture; (c) immediate prognosis; (d) ultimate prognosis.

2. Hypertension is found to be present in 25 to 75 per cent of patients who have attacks of coronary occlusion, but is not believed to be an etiologic factor in its production as it has been shown that there is a discrepancy between the incidence of occlusion and hypertension in the two sexes which is unexplainable. Although hypertension is a frequent association of coronary occlusion, there are no grounds for placing it as an etiologic factor.

3. The blood pressure probably gives the best indication of the immediate prognosis, very low systolic readings and very small pulse pressures being most ominous. In the first attack, a previous hypertension offers a better immediate prognosis, as the blood pressure is less apt to fall to shock levels.

4. The ultimate prognosis is much worse in those individuals having hypertension, as the damaged myocardium is incapable of keeping up the heart output and the minute volume is decreased. With the development of a second occlusion the already hyper-

trophied and greatly damaged myocardium is more prone to develop massive pulmonary edema.

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AN INTERESTING OBSTETRICAL CASE REPORT*

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NEW ORLEANS

This is a case which seems of unusual interest primarily because it is representative of a group of patients who are surviving today, whereas before the discovery and use of the sulfonamides and penicillin these same women would have surely expired.

This case occurred on the Independent obstetrical service of Charity Hospital. The patient was a 37 year old colored female, gravida IV, para VII, who was admitted to the delivery unit about eight p. m. on January 20, 1945. The previous obstetrical history was essentially negative with the exception of a septic early abortion in January, 1944. At this time a suspicious looking cervix was biopsied and reported as "necrosis and acute inflammatory reaction." Suggested bacteriologic studies of the cervix were, for some reason, not done. On admission a history was obtained of the membranes having ruptured 32 hours prior to hospital entry with the onset of abdominal pain and fever on the afternoon of admission. No pains had been experienced for several hours. There was no history of vaginal or other examinations before entry.

Physical examination revealed an obese colored female with a temperature of 103.6°. The blood pressure was 125/80 and the heart and lungs were clear to percussion and auscultation. On abdominal examination the uterus was found enlarged to the size of an eight months' pregnancy and was moderately tense with no intermittent contractions. No fetal heart tones were heard. Pelvic examination revealed a breech presentation, the breech lying above the pelvic inlet and the membranes ruptured. The cervix was 4 cm. dilated and thin, but rigid. Effacement was complete. A foul discharge came from the uterine cavity. The pelvis was adequate.

Laboratory work showed: Red blood cells, 4,450,000; hemoglobin, 10 grams;

*Read before the Orleans Parish Medical Society, May 14, 1945.

white blood cells, 8,700; polys. 92, 1 monocyte, 7 lymphocytes; BUN 15.4 mgm. per cent; urine negative; Kline and Kolmer were strongly positive.

During the night sulfadiazine and penicillin (12,500 Oxford units q three hours) were begun and a medical induction with pitocin given. The following morning at eight the temperature reached 105.2°. Reexamination showed that no progress had been made as was suspected from the absence of any palpable uterine contractions. The uterus, however, remained tense.

Abdominal delivery was elected and at 4 p. m., approximately 20 hours after admission, a subtotal hysterectomy, removing a stillborn fetus *in utero* along with both tubes and ovaries, was done, using cyclopropane supplemented with ether anesthesia. Upon opening the peritoneal cavity a rather large amount of thick purulent material exuded and a pool of the material was present in the cul-de-sac. A fibrino-purulent exudate was present on the surface of the fallopian tubes. Sulfanilimide crystals were left beneath the bladder flap and in the free peritoneal cavity and a drain left beneath the fascia which was closed with non-absorbable sutures. The blood pressure fell to a systolic level of 60 during the procedure and a total of 2000 c.c. of type specific blood was given. At the end of four hours the pressure was 80/40 and the pulse was 116 and of fair quality.

On the first postoperative day she remained afebrile for 24 hours. The temperature spiked to 103° rectally on the second day and gradually subsided, not exceeding 99.6° from the sixth to the twelfth day and remaining normal thereafter until she was discharged on the twentieth postoperative day.

Pathology report: Gravid uterus with attached normal placenta and umbilical cord; acute suppurative and chronic endometritis; acute suppurative salpingitis and perisalpingitis; acute suppurative perisalpingeal pylephlebitis; corpus luteum, follicular cysts and corpora albicantia of ovaries.

Blood culture on April 21, 1945, was negative. Culture from peritoneal cavity showed *Staphylococcus aureus* pyogenes and non-hemolytic streptococcus. A culture taken from the cervix during convalescence grew an anaerobic streptococcus.

DISCUSSION

Dr. Adolph Jacobs (New Orleans): Having occurred in the independent service, Dr. Callender consulted me regarding this case. Usually we get in communication with the residents by telephone. I must say now that we are fortunate during this emergency to have capable residents because it is almost impossible for us to go very often to the hospital, particularly at night when we ourselves need rest. In this instance Dr. Callender asked me—although he consulted me frequently over the telephone and I would agree with him about the procedure—he asked that I see the case. We were faced with a real problem there. Because of the history we realized the infection evidently occurred in the cervix and was a latent infection. The fetus was not macerated and evidently the flare-up occurred only a short period prior to admission of the patient to the hospital. Having been convinced that the fetus was dead, it was a problem as to procedure. Now before the advent of penicillin and the sulfa drugs we may have been tempted to do something from below and in this case that would have been fatal. The cervix was high and rigid. I think a great deal of credit is due to Dr. Callender for the way he handled this case from the very beginning; giving the patient penicillin and sulfa drugs prior to the cesarean section.

Dr. Woodard Davis Beacham (New Orleans): Dr. Callender discussed this case with me after the paper had been written. He commented on the fact that the dosage of penicillin was rather small. That can be explained on the basis that penicillin was not as easily obtainable then, as it is at the present time. It is our opinion that cases of this type should receive a large initial dose of penicillin. As a matter of fact, we suggest that such cases receive ordinarily 50,000 Oxford units as the initial dose. The chemotherapeutic agent may be administered intravenously, or intravenously and intramuscularly. Thereafter the penicillin should be given intramuscularly at intervals of three or four hours in doses of 25,000 Oxford units. The management of this case was entirely correct. If a Watters' extraperitoneal section had been done the peritonitis could not have been combatted as efficiently as it was in this instance.

All of us appreciate the advisability of employing sulfonamides in addition to penicillin in these cases; appreciating the fact that some organisms are resistant to penicillin and responsive to sulfonamides and vice versa.

I wish to compliment the chiefs of the Independent Obstetric Service, Dr. Jacobs, and Dr. Callender, for saving a patient who could have very easily been an obstetrical mortality. Proper

antenatal care has as one of its aims the prevention of complications of this type. If this patient had been admitted to the hospital earlier, it is probable that she would not have lost her uterus, and with good antenatal care, her baby would have been saved.

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THE VALUE OF INFLUENZA VACCINATION

MITCHELL EDE, M. D.
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Since R. E. Shope in 1931 established the fact that a filtrable virus is the essential factor in the production and transmission of the disease influenza, many workers have sought to find an efficacious vaccine to prevent future epidemics of influenza. The results of these studies have been conflicting and inconclusive. The object of this paper is to review the work which has been accomplished and, if possible, to derive some definite conclusions as to the value of the vaccines prepared to date.

VACCINES

The strains of influenza virus used in preparing the vaccines were the PR 8 strain, the Melbourne strain isolated in 1935, the W.S. strain which was isolated by Smith and Laidlow in 1933, and the Lee strain of influenza virus Type B isolated in 1940. The above strains were tested singly in a vaccine and in combination with each other by the different researchers.

PREPARATION

The virus was grown on tissue culture medium and in mouse lungs before 1940. Since 1940 the virus used for vaccine has been grown on the chorio allantoic membrane or in the allantoic fluid of the developing chick embryo. Those chick embryos of 10-12 days' age were considered to be the optimum ones to use. The virus following cultivation was used in one of two ways:

1. As active attentuated virus
   a. Unconcentrated
   b. Concentrated *or*
2. As inactivated virus
   a. Unconcentrated
   b. Concentrated

Formalin was used to inactivate the virus. A number of methods have been developed to concentrate the virus but only that developed by Hirst and co-workers will be described because this method, in my opinion, is the best. By this method a ten-fold[1] concentration of virus can be obtained. The procedure is as follows:

One liter of frozen allantoic fluid containing the virus desired is carefully thawed. A precipitate is formed which carries down with it 90-95 per cent of the virus. This precipitate is removed by centrifugation at 1000 r.p.m. for 10 minutes. The temperature of the fluid does not rise appreciably above 0° during this procedure. The sediment is then resuspended in 100 c.c. of the supernatant fluid and this gives a ten-fold concentration. The virus can then be inactivated by the addition of formalin.

The usual procedure for attenuating the virus was by animal passage. The ferret was used. Also passage through chick embryo was found to reduce the pathogenicity of the virus.

WHICH MODE OF PREPARING THE VACCINES AS MENTIONED ABOVE IS BEST

Hirst, Rickard, Whitman, and Horsfall[2] experimented with the various preparations and reached the conclusions: 1. "Within certain limits the mean antibody response of human beings increased as the amount of virus injected was increased. When large amounts of influenza virus were given, the antibody response was of the same order of magnitude as that which occurred following actual infection by this virus." This would indicate that the concentrated forms of vaccine would produce better results than the unconcentrated ones. 2. "There was no significant difference in the antibody response of human being given active virus or inactivated virus as long as both types had approximately the same number of virus."

The above results may explain the failure of vaccines used by individuals when the vaccine used was not concentrated.

CORRELATION BETWEEN NEUTRALIZING ANTIBODIES IN SERUM AGAINST INFLUENZA VIRUSES AND SUSCEPTIBILITY TO INFLUENZA IN MAN

Before proceeding further, the correlation between neutralizing antibodies in the serum and susceptibility to influenza in man should be mentioned in order to clarify the

following discussion and to make its understanding easier for the reader.

In many of the experiments the level of antibody in the serum was used as the measure of value of the vaccine by the researchers because it was a method which was practical. By studying the serum level it would be possible to follow the effects of the vaccine. They found that a rise in the antibody level did occur following vaccination and the question then arose that if the efficacy of the vaccine was to be determined by the height and duration of rise of the antibody level in the serum, then what was the correlation between high serum levels of antibody and immunity to influenza.

In work done by Rickard and co-workers[3] it was shown that during an epidemic that the attack rate was higher among those individuals who had low levels of antibody in their serum. The same workers[4] showed that the level of neutralizing antibodies in the serum against the homologous virus is an important factor in determining susceptibility or resistance to the disease. They showed that high levels of antibody against influenza virus Type A would protect against Type A virus but did not afford any protection to influenza virus Type B and this in itself is proof that the circulating antibodies do play a part in immunity.

That neutralizing antibody is not the only factor responsible for determining whether the individual will contract the disease is evident in view of the fact that persons possessing high antibody levels do contract the disease. However, the attack rate is lower among these individuals than among those with lower antibody levels in serum.

The fact that those with high antibody level in the serum still contract the disease may be accounted for by two factors which play a part in immunity. (1) The anatomy of the upper respiratory tract in these individuals may be such as to prevent intimate contact between virus and circulating antibodies. (2) Since influenza is assumed to be transmitted from one person to another by means of virus-containing droplets, it is reasonable to conceive that individual exposure in an epidemic may be variable and one person may come in contact with small quantities of the virus and another may inhale a large amount.

From the above it may be concluded that there is a positive correlation between the level of the antibody in the serum and the susceptibility of the individual to the disease. But the correlation is not absolute for the antibody level is only one of many factors entering the picture. For practical purposes, however, I think we can use the level of antibody response to a vaccine as a measure of the efficacy of the vaccine. The level is probably the most significant single factor determining whether infection does or does not occur. A disturbing and as yet little studied and unexplained fact is the fact that influenza of unknown cause appears to occur with somewhat increased frequency among individuals who possess considerable concentration of antibodies against both known influenza viruses.

SPECIFICITY OF ANTIBODY RESPONSE OF HUMAN BEING TO STRAINS OF INFLUENZA VIRUS

As mentioned above in discussing correlation between antibody level and susceptibility of the individual, high antibody levels against influenza A virus do not diminish the frequency of influenza B; nor do high antibody[5] levels against influenza B virus reduce the incidence of influenza A.

Bodily and Eaton vaccinated individuals with influenza Type A virus and later tested their sera against the various strains of human influenza (PR 8, Melbourne, W.S.) and swine influenza—an increase in antibodies of four-fold or over to PR 8 occurred in 61.6 per cent, to Melbourne in 71.1 per cent, to W.S. in 34.4 per cent and to swine in 30.7 per cent. This would indicate that the immune response was apparently not broad enough to produce significant antibody increases to W.S. and swine influenza. This would also indicate that there was almost complete reciprocal cross immunity in human sera between PR 8 and Melbourne strains. However, this is not entirely true for there was a certain amount of specificity in the antibody response as was demonstrated by experiment with the two strains. Fifteen persons vaccinated with Melbourne virus showed a better reactivity against

Melbourne strain than against PR 8, as indicated by agglutinative or mouse neutralization tests. On the other hand, sera of 25 persons vaccinated with PR 8 virus vaccine showed a greater reactivity against PR 8 by mouse neutralization tests and agglutinative tests than to the Melbourne strain. The fact that both PR 8 and Melbourne type antibodies were increased as much as they were when the influenza virus A isolated from the 1940 epidemic was used to vaccinate the people may be explained by the fact that this vaccine possessed antigenic components common to these strains.

These findings indicate that immune response of human beings to strains of type A influenza virus is not sufficiently broad to guarantee protection against infection with all viruses within the type A group when one strain is used in the vaccine.

METHODS OF ADMINISTRATION

The two main methods of administering the vaccination have been by the intranasal and subcutaneous routes. Most of the work done with the intranasal method has been carried on by Australian workers, while the workers in this country have advocated subcutaneous vaccination.

EXPERIMENTAL RESULTS WITH INTRANASAL VACCINE

D. R. Bull and F. M. Burnet,[6] using 107 soldiers as subjects, vaccinated them by the intranasal method with a vaccine consisting of the Melbourne and W. S. strains. Following the vaccination they found that for each type of virus, from 68 to 80 per cent of the subjects showed no significant change in antibody level. Twenty to 30 per cent showed an increase in antibody level. Also, those having lower initial antibody level showed a higher rise in antibody level. Taken at face value these results appear to be inferior to those obtained by American workers with subcutaneous inoculations of adequately high titer of virus. Bull and Burnet held that it must be remembered that the intranasal vaccine can be expected to "take" only in those subjects who are susceptible to influenza virus infection. for in the great pandemic of 1918 about 70 per cent of persons escaped clinical infection. Therefore even with an ideal vaccine of this type you would not expect more than 30 to 50 per cent of subjects to show a definite rise in antibody level against any one type. They maintain that the existence of a real resistance in some persons to infection by attentuated strains is strikingly shown by the failure in most instances of repeated re-inoculations to provoke a rise in antibody level in those subjects who fail to respond with such a rise to the first inoculations. In substantiation of this statement the following experiments are given.

D. R. Bull and F. M. Burnet[7] experimented on 23 individuals chosen for low antibody titer against influenza Type B and vaccinated with Type B. Twenty-one of the 23 showed a significant rise in antibody level. Only two showed a significant rise following the second administration three to six months later. They hold that this represents a real resistance to infection induced by this procedure. In another experiment 14 subjects with antibody level between 35 and 90, 12 of whom in response to the first inoculation showed significant rises; of 11 in the same range (35-90) inoculated for the second time, two only showed significant rises. The reasonable deduction is that the experience of one inoculation has produced a resistance by one mechanism or other greater than would be gauged from a consideration of Hirst antibody levels alone, and this resistance is great enough to produce immunity.

J. Mawson and C. Swan[8] claim that the use of living, attenuated influenza virus strain intranasally gives as good results as does subcutaneous injection of the virus. However, Hirst, using a ten-fold concentration of virus[9] produced a six-fold rise in antibody level using subcutaneous vaccination while Mawson and Swan got only a two-fold rise with intranasal vaccination. However, Mawson and Swan consider that there is a possibility that the resultant mild infecfection of nasal tissues will lead to an increase in local resistance not obtained by subcutaneous injection. The value of this intranasal vaccination must yet stand trial in an epidemic. Until such a time, when the vaccine can be given in or before the spread

of an epidemic, no definite evaluation can be made.

UNFAVORABLE EVIDENCE OF VALUE OF INTRANASAL VACCINATION

T. Francis, Jr.,[10] infected 30 individuals with influenza Type B by placing the individuals in a room in which the virus had been finely dispersed. Twenty-four of them came down with a clinical infection resembling a mild form of the disease. Four months later 24 of the same subjects received a second inhalation of the same virus. Fever, symptoms and serologic responses were noted for a second time. Although the illness was milder in those previously infected than in controls inoculated at the same time, few of those previously infected were refractory to inoculation. The question arises, if frank infection fails to give a uniform staunch resistance over a period of four months, can a single exposure to a much milder single stimulus by the same route have a greater effect. This hardly seems likely. From this study the suggestion is derived that for intranasal vaccination to be effective it should be repeated at intervals shorter than four months.

As mentioned above, Bull and Burnet consider the failure to show a rise of antibody level on re-inoculation as evidence of real resistance to infection. Francis disagrees and holds it in doubtful significance as he says an increase in antibody after re-inoculation may not occur even with sharp clinical response.

At the present it may be said that the value of intranasal vaccination is questionable and uncertain. It must be evaluated in the light of its ability during an epidemic. In the face of the work of Francis it can hardly be expected to produce an immunity of longer than three months. We do know that it does cause a rise of antibody level which is of a significant amount for at least three weeks. The intranasal vaccination does have certain advantages: (1) It causes trivial symptoms, and (2) it is simple to prepare—it can be made more rapidly and requires less time, skilled man power and material and in the face of an epidemic this would be very important.

HISTORY

In 1933, Smith, Andrewes, and Laidlow[11] obtained a virus from an influenza patient. Following this association of a virus with influenza, work was begun in hope of obtaining a vaccine which would afford protection from this disease. Experimental work on animals by the same authors[12] showed that ferrets following infection were resistant to reinfection by artificial inoculation of the virus into their respiratory tract. Francis and Magill[13] confirmed this work. In 1936 and 1937 Francis and Magill[14] further showed that the subcutaneous injection of active influenza cultivated on tissue culture medium produced a rise in antibody response in humans. The circulating antibodies persisted for five months at a higher level than was initially present before vaccination but it was highest two weeks following vaccination.

The first experiment which gave any light on the protective effect of vaccination against influenza in man was reported in 1937. First, Stokes, Chenowith, Waltz, Gladen, and Shaw[15] and later, Stokes, McGuiness, Langner, and Shaw[16] conducted experiments using active culture virus. It was found that the incidence of the disease was lower among those who had received subcutaneous vaccination than among the controls. The latter group of workers found that in those groups who were vaccinated a short time before the epidemic occurred showed a lower attack rate than in those groups vaccinated a longer time before the epidemic.

Unfavorable results were obtained by Smith, Andrewes, and Stuart-Harris[17] following vaccination of several groups of individuals with a formaldehyde inactivated virus prepared from infected mouse lungs. A true evaluation of the vaccine could not be made because of the appearance of an epidemic a few days after vaccination. They found though that there was no essential difference between the attack rate among those vaccinated and not vaccinated, who developed influenza two weeks after vaccination. However, the same strain of virus isolated in the epidemic was not anti-

genically identical with the virus in the vaccine. This accounts for the failure in this case for it was shown as mentioned above by Bodily and Eaton that there was a specificity of antibody response in human beings to strains of influenza virus.

R. M. Taylor and M. Dreguss[18] carried out an experiment in 1937 using the same type vaccine as that used by Smith, Andrews and Stuart-Harris. They vaccinated 306 persons with a formaldehyde inactivated influenza virus. Their results were also disappointing as the attack rate among the vaccinated was not appreciably lower than the attack rate among the controls. The epidemic occurred 17 days after vaccination which, had the vaccine been of value, would have been the period when the antibody level of the blood was highest. The authors offered two reasons for the apparent ineffectiveness of the vaccine. First, whether one injection of the virus preparation is sufficient to increase adequately resistance to natural infection, even against a virus strain which is antigenically identical to the one used in the vaccine. Second, the antigenic difference between the virus used in the vaccine and the viruses responsible for the epidemic may have been different.

In the epidemic of influenza A in 1939, the formalinized W.S. virus vaccine again failed to give protection.[19] Siegel and workers[20] also found that the formalinized virus grown on tissue culture afforded little protection. "The vaccine was given three months before the epidemic. The results were considered inconclusive because there was serological evidence of the prevalence of influenza A and other unrelated acute infections of the upper respiratory tract which were clinically indistinguishable."

From the above data it can be seen that before 1940 the clinical trials in which either formalin-inactivated, active mouse-lung virus, or active tissue culture virus were employed, the incidence of clinical influenza was not significantly different in those receiving subcutaneous vaccination and those not vaccinated.

CLINICAL RESULTS OF 1940-1941 EPIDEMIC

In the following 1940-41 epidemic, the vaccine used for the most part was the complex vaccine of Horsfall and Lennette, which consisted of formalin-inactivated PR 8 strain of influenza A virus and canine distemper X virus propagated simultaneously in the developing chick embryo.[21] Clinical tests of its prophylactic value during the 1940-41 epidemic were made and the results have been conflicting.

During the 1940-41 epidemic of influenza A in this country, a number of researches were carried out. W. P. Martin and M. D. Eaton[22] took a complex formalinized ground chick embryo vaccine containing canine distemper and influenza A virus and another vaccine made from active influenza A strain Melbourne in chick embryo suspended in saline and used these two vaccines prophylactically during a recent influenza outbreak in two institutions. The active tissue culture vaccine is called V-1 and the complex inactive vaccine V-2. Table 1 gives the results. The epidemic occurred within two weeks following vaccination.

TABLE 1

	Institution X			Institution Y		
	Total in Group	Total Cases	Incidence Per Cent	Total in Group	Total Cases	Incidence Per Cent
Vaccine 1	193	16	8.3	169	10	5.9
Vaccine 2	223	12	5.4	244	18	7.4
Total vaccinated	416	28	6.7	413	28	6.8
Controls	4560	365	8.0	2487	385	15.5

It can be seen from Table 1 that at Institution Y that the difference in incidence of cases between the vaccinated and control groups is sufficiently great to be of some significance especially since the incidence of influenza A was high in this institution. The failure of V-2 to give adequate protection can be attributed to the short lapse of time between vaccination and peak of the epidemic. The failure of V-1 to produce some immunity in Institution X is unexplained.

Brown and Eaton, using a ground chick embryo vaccine, reported during the epidemic of 1940-41 a reduction in attack rate of 50 and 60 per cent in two hospital groups. The significant factor brought forth by the last two mentioned experi-

ments is that these favorable results were obtained in epidemics which occurred shortly after vaccination was performed.

Contrary to the favorable reports given above, work carried on in New York by Dolldorf and co-workers,[23] using the same type vaccine, showed no significant difference in the incidence of clinical influenza and influenza A among vaccinated and non-vaccinated individuals. Seventy-five per cent of their cases had serologic reports and 70 per cent were positive for influenza A. There was no evidence of influenza B.

The results of Dolldorf were supported by the results of Siegel and co-workers[24] who, using the same vaccine employed in studies at Letchworth Village, failed to reduce the incidence of respiratory illnesses serologically related to influenza A in the epidemic of January-February, 1941.

The last two experiments had an interval of six and eight weeks, respectively, between vaccination and epidemic which may be the factor responsible for the failure. In those experiments using the same vaccine in which the interval was short, the vaccine proved of value in producing immunity.

Horsfall and co-workers[25] used the same preparation. They reported a series in which the interval between the vaccination and the epidemic was four months. They obtained an attack rate reduction of 25 per cent on a clinical basis. The results cannot be used upon which to draw definite conclusions because the results in individual institutions showed such enormous variations, well beyond the sampling error.

Hirst and co-workers showed that the greater the number of virus the vaccine contained the greater would be the antibody response in the vaccinated individual. This lead the researchers next to the use of concentrated vaccines. That described by Hirst and mentioned early in this paper is only one of a number of methods for concentrating the virus but a description of other methods is beyond the scope of this paper.

DETERMINATION OF THE EFFICACY OF SUBCUTANEOUS VACCINATION IN PREVENTING EXPERIMENTAL INFECTION OF HUMAN BEINGS

In the absence of an influenza epidemic in 1941-42 and 1942-43, a group of new vaccines which contained influenza virus, concentrated and inactivated were treated by artificial experimental infection of human beings. Smorodintseff and co-workers[26] have shown in a number of human volunteers that inhalation of active influenza A virus may lead to disease. It was hoped that similar inhalation experiments performed on vaccinated and non-vaccinated human beings could give some additional information about the value of these vaccines.

Henle and co-workers[27] used a vaccine which consisted of an equal mixture of allantoic fluids infected with PR 8, W.S., and Melbourne strains of influenza virus A. The virus was inactivated by formalin; 72 individuals were used as subjects; 28 were used as controls and not vaccinated; 27 were vaccinated four months before exposure to the virus; 17 were vaccinated two and a half weeks before exposure. The subjects were exposed in a room to active influenza A virus which they inhaled. Of 28 control individuals, 10 came down with clinical influenza. Only one case which had not responded to vaccination occurred among the 44 vaccinated persons, 27 of whom had been immunized four months prior to exposure. There were, however, numerous subclinical cases in the experiment. A good correlation between the pre-inhalation antibody level and the degree of protection is indicated in that most cases occurred in the group with the lowest antibody titer.

Henle's experiment indicated that the concentrated inactivated vaccine induced an effective immunity four months later. This length of immunity had not been produced before and the report stands out as the results of this vaccine were remarkably effective.

As in 1941-42, no epidemic of influenza occurred in 1942-43. Francis and co-workers[28] had made rather extensive studies for the purpose of determining the value of subcutaneous vaccination with inactivated concentrated influenza virus against the natural disease in man. The anticipated

outbreak of influenza however did not occur but they had the opportunity to test the resistance of certain of the vaccinated individuals to induced infection.

In their experiment they used a vaccine containing the PR 8 strain of influenza virus A and the Lee strain of influenza virus B. The virus was concentrated and inactivated. The subjects were 102 individuals. On December 21, 1942, 45 received 1.0 c.c. of the vaccine subcutaneously. On April 21, 1943, 17 of these men again received 1.0 c.c. of the vaccine as did 21 men not previously vaccinated. There remained 28 men who had been vaccinated four months earlier and 36 individuals who had not received the vaccination. On May 4, 1943, 13 days after the last administration of vaccine, the entire group received an intranasal spray of Type A influenza virus in allantoic fluid.

It was found upon analysis of the results that temperatures of 100° or more were observed in 50 per cent of the controls, in 32 per cent of those vaccinated four and a half months before exposure, in 14.3 per cent of those vaccinated two weeks before and in 17.6 per cent of those vaccinated four and a half months and two weeks before. None of those vaccinated two weeks before infection had temperatures higher than 100° while nine of the control and three of the men vaccinated four and a half months earlier had fever of 101° or higher. The results indicate that the vaccine employed induced a state of resistance, manifested in reduced febrile responses, to intranasal infection with influenza virus Type A. It was most effective in those vaccinated two weeks before exposure. The protective influence of vaccination declined considerably four months later. This experiment agrees with that of Henle described above in showing that subcutaneous vaccination clearly exerts a beneficial influence against induced infection with influenza virus, Type A. It differs in showing effective immunity was considerably reduced four months later. Francis believes that the virus Henle and co-workers used was not as virulent as the one he used and that in the face of an epidemic many of the cases they reported as subclinical would be clinical cases.

Salk and co-workers[29] performed essentially the same experiment as that described by Francis above, except they exposed the individuals to influenza Type B instead of Type A. They found that this vaccine containing concentrated and inactivated influenza virus Type A and B was capable of exerting a protective influence, as measured by febrile response, against induced infection of Type B influenza for at least four months.

RESULTS OF EXPERIMENTAL WORK DURING EPIDEMIC 1943-1944

In the autumn of 1943 the members of the Commission on Influenza and associates with T. Francis, Jr., as director, carried out a controlled clinical trial[30] to determine the prophylactic efficacy against epidemic influenza of a concentrated inactivated vaccine containing the viruses of influenza Types A and B. It had already been shown by the last two preceding experiments described above that a vaccine similarly prepared was capable of furnishing definite protection against experimental induction of influenza A or B. The vaccine consisted of the PR 8 and Weiss strain of influenza virus Type A and the Lee strain of Type B. They used control material consisting of isotonic solution of sodium chloride to which formaldehyde was added. The subjects were members of ASTP units in eight universities over the country and a ninth unit comprising members of the ASTP units of five New York medical and dental colleges. Each unit was divided in half so that one-half received the vaccination and one-half the control material. The following Table 2 shows the results:

TABLE 2

Total Number	No. of Subjects Vaccinated	Control	No. of Cases Vaccinated	Control	Incidence Per Cent Vaccinated	Control	Per Cent Total Cases Vaccinated	Control
12,474	6263	6211	138	442	2.22	7.11	23.8	76.2

It is seen that the incidence of clinical influenza in 6211 men receiving control material was 7.11 per cent, while in the 6,263

receiving vaccine there was an incidence of 2.22 per cent, a ratio of 3.2 to 1. The significance of the results is heightened by the uniformity of trend in practically every unit.

The difference between vaccinated and control individuals was greatest at the height of the epidemic curve. Before the epidemic reached its peak and following the peak the difference between the two groups was less.

That the vaccine becomes effective about one week after inoculation is well illustrated in the results reported from the University of Iowa and the College of the City of New York. In these units the vaccine was given after the epidemic started. The attack rates were not different very much during the first week after vaccination but then it diverged sharply.

TABLE 3

University of Iowa

Epidemic: Nov. 29, 1943
Dec. 25, 1943
Vaccination: Dec. 2-4, 1943
Number in study:

Vaccinated	599
Control	599
Total	1198

Cases by weeks ending

	Vaccinated	Control
Dec. 11	3	12
Dec. 18	2	16
Dec. 25	4	11
Jan. 1	2	1
Total Cases	11	40
Incidence Per Cent	1.83	6.67
Per Cent of Total Cases	21	79

C. C. N. Y.

Epidemic: Nov. 7, 1943
Dec. 18, 1943
Vaccination: Nov. 19, 1943
Number in study:

Vaccinated	1050
Control	1055
Total	2105

Cases by weeks ending

	Vaccinated	Control
Nov. 11	33	27
Dec. 4	8	52
Dec. 11	6	17
Dec. 18	0	6
Total Cases	14	75
Incidence Per Cent	1.33	7.11
Per Cent of Total Cases	16	84

It may be said from the results that if the vaccine is given a short time before or after the epidemic has started it will afford protection as seen by the fact that the attack was 2.22 among those vaccinated and 7.11 among the controls. The vaccination produced its maximum effect at the height of the epidemic.

This experiment gives us no information as to the duration of the protective value of the vaccine.

Studies in human immunization with a similar vaccine as used by the Commission were conducted by Hirst, Rickard and Friedewald.[31] They reported the results of a study of the efficacy of this vaccine when the period between vaccination and epidemic was about one year. Since the report of the Commission gave no indication of the duration of immunity with this concentrated, inactivated vaccine, the report of Hirst, Rickard and Friedewald may be considered as an extension to their observations.

The vaccine used consisted of PR 8 strain of influenza A and the Lee strain of influenza B. In one institution, the vaccine was made with the PR 8 and W.S. strain of influenza A only. The vaccine was concentrated and inactivated. The subjects were taken from seven penal institutions in widely separated states. Only those who volunteered were vaccinated and the rest were used as controls. Vaccination was given in November and December of 1942 and no epidemic occurred until the winter of 1943. This gave an interval of from 11 to 14 months between vaccination and epidemic. Serologic tests were run on the individuals so that the antibody level in the blood could be followed. Among the 2945 vaccinated, the attack rate was 3.6, while among the 4451 the attack rate was 5.5, a difference of 35 per cent. In all seven institutions, the attack rate was consistently lower among the vaccinated than in the controls. They found on serological examination that the vaccination resulted in a high order of antibody response within two weeks after injection which declined rapidly by the sixth and seventh week but then persisted at a low level for a year. At one year the great majority of individuals vaccinated had antibody levels much higher than their pre-vaccination titer. The average reduction in attack rate was about 35 per cent.

However, the protection afforded by the vaccine after two months' lapse of time cannot be considered sufficient for practical purposes for the number of vaccinated individuals who contracted influenza after one year was still too high.

SUMMARY

The object of this paper was to determine the value of the influenza vaccination. A review of the literature was made in an attempt to determine whether vaccines were of practical significance in the field of preventive medicine. The widespread realization of the danger and destruction which was wrought by the great pandemic of 1918 has lead many workers to search for a vaccine which would provide men with an adequate weapon to fight off such a recurrence. Many workers in Australia, England, and the U. S. have devoted much time in intensive research, in developing and testing different vaccine preparations, discarding old ones, preparing new ones, ever looking for one which would stand up in the face of a virulent attack of the influenza virus. This paper brings you in a brief form the search, the toil, the trials, failures, and successes of these workers.

As mentioned above many vaccines have been prepared in many forms and they contained different strains of influenza virus. The different strains used for the most part were the PR 8 strain, the Melbourne strain, the W.S. strain of Type A virus and the Lee strain of Type B virus. The vaccine was used in either inactivated or attenuated form—concentrated or unconcentrated.

In many of the experiments the workers determined the efficacy of the vaccine by the height and the duration of rise of the antibody level in the serum because it was shown that there was a positive correlation between the level of the antibody titer in the serum and the susceptibility of the individual to the disease. Although the correlation is not absolute, it can still be used for it was proved that the level is the most significant single factor determining whether infection does or does not occur.

An important step in the advance to find a good vaccine was the illustration of the specificity of antibody response of human beings to the different strains of influenza virus. From this it may be reasoned that, to prepare a vaccine which would afford protection against all strains of the influenza virus, the vaccine would have to contain the many strains.

In 1936 and 1937 experimental work showed that the subcutaneous injection of active influenza virus cultivated on tissue culture medium produced a rise in antibody response in humans which lasted for five months. This type vaccine, which was an active attenuated one grown on the tissue culture medium, was first tested in the face of an epidemic in 1936-1937 by Stokes and co-workers in two separate experiments. They found that the incidence of the disease was lower among those who had received subcutaneous vaccination than among the controls, and that those groups vaccinated a short time before the epidemic occurred showed a lower attack rate than did those groups vaccinated a longer time before the epidemic.

During the same period, Smith, Andrewes and Stuart-Harris, using a formaldehyde inactivated virus prepared from infected mouse lungs, obtained unfavorable results. They found that there was no essential difference between the attack rate among those vaccinated and not vaccinated, who developed influenza two weeks after vaccination. The value of these results in arriving at any conclusions as to the value of the vaccine is questionable as the strain of virus isolated in the epidemic was not antigenically identical with the virus in the vaccine. Taylor and Dreguss, using the same vaccine as did Smith above, found that during the 1937 epidemic of influenza in Hungary, the vaccine produced no immunity.

In the epidemic of 1937, this same type vaccine again failed to give protection either in England or in the United States. The period between vaccination and epidemic was three months.

From the above it can be seen that before 1940 the clinical trials in which either for-

malin-inactivated, active mouse lung virus or active tissue culture virus were employed, indicated that the incidence of clinical influenza was not significantly reduced by vaccination where the period between vaccination and epidemic was over three weeks.

It was shown by Hirst and co-workers that the greater the number of virus contained in the vaccine the higher would be the antibody titer rise and the rise would be of longer duration following vaccination. Therefore, an attempt was made to improve the concentration of the vaccine. Horsfall and associates found they could cultivate the virus in the growing chick embryo and the vaccine prepared from this chick embryo, which was ground up, contained a higher concentration of the virus than did those vaccines previously used.

This vaccine was tested clinically during the 1940-1941 epidemic of influenza A in this country. It contained the PR 8 strain and the swine influenza virus. The results reported were conflicting.

Only Martin and Eaton and Eaton and Brown reported experiments with this vaccine in which a significant reduction in attack rate followed vaccination. Martin and Eaton reported an attack rate reduction of 32 per cent and 52 per cent in two institutions. Brown and Eaton reported reductions of 50 to 60 per cent. In their experiments the period between vaccination and epidemic was only two weeks.

When the interval between vaccination and epidemic was from six to eight weeks, as was the case in the experiments of Dalldorf and in that of Siegel, it was found that this same vaccine produced no reduction in the attack rate.

The work of Horsfall who reported a much larger series with a reduction in the attack rate of 25 per cent cannot be used to draw conclusions from, as there was an enormous variation in the individual institutions which were beyond the sampling error.

Because there were no epidemics in the winters of 1941-1942 and 1942-1943, experiments were carried out by artificially infecting individuals who were vaccinated. The vaccines used during this period contained virus grown on the allantoic fluid of the growing chick embryo. The virus was inactivated and concentrated. Henle found that this vaccine produced an effective immunity for four months. Francis confirmed Henle's work that the vaccine induced an immunity but he disagreed with Henle in that he does not think it confers immunity for such a long period of time. He holds that Henle in his experiments had many subclinical cases which in the face of a more virulent organism would have been clinical cases.

In 1943 the Commission on Influenza carried out a controlled clinical trial to determine the prophylactic efficacy against epidemic influenza of a concentrated inactivated vaccine similar to the one used above by Henle and Francis. The vaccine had already been proved capable of furnishing protection against experimental induction of influenza A or B. The vaccine was given shortly before or during the epidemic. They found that the vaccine did produce immunity as was shown by the fact that 2.22 per cent of those vaccinated showed clinical evidence of influenza while 7.11 per cent of those not vaccinated came down with the disease. The vaccine was found to be most effective about one week after inoculation.

As this experiment gave no indication as to the duration of effectiveness of the vaccination, Hirst and co-workers carried out an experiment in which the duration between the vaccination and epidemic was from 11 to 14 months. They used a vaccine which was similar to the one used by the Commission. Serologic evidence of their subjects indicated that vaccinated individuals had on the order of three times as much circulating antibody at the time of the epidemc as they had before vaccination. They found that the attack rate among the vaccinated individuals was lower than among those not vaccinated. However, Hirst holds that the protection obtained after two months' lapse of time is insufficient for practical purposes.

The above experimental results indicate

that in the epidemics of 1940-1941 and 1943-1944 there was a reduction in attack rates when the formaldehyde inactivated vaccine was given shortly before or early in the beginning of the epidemic. There was no immunity four weeks after the inoculation of the preparation which was used in 1940. The concentrated vaccines used in 1943-1944 were more potent than those used in 1940. Maximum effectiveness was at two weeks at which time there was a sharp fall in effectiveness which however lasted at a low level for a year.

In view of the above facts, it can be seen that at the present time there is still no vaccine which will produce an immunity for a longer period than four weeks. Since it has been shown that immunity is produced within eight days following vaccination, it appears that from an economical view point and in view of the fact that it is impossible to predict the occurrence of an epidemic, it seems that at present the wisest thing to do would be to give the vaccination after the epidemic has begun and the causative virus determined.

As shown by Salk and co-workers, and Mawson and Swan, vaccination against influenza virus Type B either by the intranasal or by the subcutaneous method will produce effective immunity for a period of four months. It may be said that the problem at present concerns the production of immunity to influenza Type A virus.

CONCLUSIONS

The following conclusions have been drawn from the experiments and data described in this paper:

1. The greater the number of virus contained in the vaccine the more potent will be the preparation.

2. There is no significant difference in the antibody response of human beings to active or inactivated virus vaccines.

3. There is a positive correlation between the level of antibody in the serum and the susceptibility of the individual to the disease. The correlation is not absolute as there are other factors which play a part in the immunity to influenza but the level of the circulating antibodies is probably the most significant single factor determining whether infection does or does not occur.

4. There is specificity of antibody response in human beings to the different strains of the influenza virus and therefore if the vaccine is to protect against any certain strain of influenza virus then the vaccine must contain that particular virus strain.

5. Conclusions as to the efficacy of the intranasal method of vaccination cannot be drawn until the method has been tested in the face of an epidemic. It does have the advantage of being easily and quickly prepared.

6. The use of the concentrated vaccine subcutaneously will produce definite immunity for a period of four weeks. It is most effective two weeks after vaccination. Immunity can be expected eight days following vaccination.

7. From an economical point of view it would be best to give the vaccine after the outbreak of the epidemic. This is best because it is hard to predict the appearance of an epidemic and because immunity can be expected within eight days.

8. Immunity to influenza Type B can be established by vaccination for a period of four months, following vaccination with a concentrated vaccine containing influenza. The main object now is to find a vaccine which will give immunity to influenza Type A for a longer period than four weeks.

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CLINICO-PATHOLOGIC CONFERENCE

GRANVILLE BENNETT, M. D.
CHICAGO, ILL.
and
EDGAR HULL, M. D.
NEW ORLEANS

CASE SUMMARY

The following clinico-pathologic conference was presented before a meeting of the Orleans Parish Medical Society.

E. W., a colored female, 14 years, was admitted on April 21, 1943 and expired on May 11, 1943.

C. C. **Fever.**

P. I. **The patient became ill on March 8, 1943, with crying spells and irritability. Two or three days later her feet, legs and arms began to swell. Several days later she broke out in a rash over the entire body, including the face and extremities. The lesions first appeared as blisters the size of a dime. The swelling lasted some two weeks before gradually disappearing. The skin lesions persisted, though were improving. Since the beginning of her illness the patient had fever. She had spells of nervousness, extreme irritability and voluble talking spells. On April 19 the patient began vomiting and the mother noticed streaks of blood in the vomitus. The patient believed she lost considerable weight since the onset of the present illness.**

P. H. **The patient has always been in good health. She had had the usual childhood diseases.**

***Physical Examination*:** **The patient was a well developed and well nourished colored girl who appeared older than her stated age of 14. She appeared acutely ill, talking irrationally at times. The head revealed no abnormality. The pupils were equal and regular and reacted to light and accommodation. A scaly eczematous lesion was noted on the lobe of the left ear. The lips were parched. Many mucous patches were present on the palate. The pharynx was clear. The neck was pliable with no masses. The skin was dry and hot. There were numerous healed and partly healed lesions over the entire body, particularly the chest and lower extremities. There were several scaly lesions on the upper extremities. These were covered with crusts. The lymph nodes were not enlarged. The lungs were clear to auscultation and percussion. The heart did not appear enlarged and the heart tones were of good intensity. The rhythm was regular; the rate rapid. No murmurs were heard. The abdomen was not distended and there was no tenderness or rigidity. No organs or masses were felt. Genitalia showed a slight amount of whitish purulent discharge. On pelvic examination there was tenderness and a mass felt**

on the left side. The cervix was small and not easily moved. The extremities showed no deformities or paralyses. Reflexes were physiological.

Laboratory Findings: Blood count on April 22, 1943, showed hemoglobin 11 grams, red blood cells 3,860,000, white blood cells 12,800, 64 per cent polymorphonuclear leukocytes and 36 per cent lymphocytes. On May 5, 1943, hemoglobin was 8.5 grams, red blood cells 2,500,000, white blood cells 4,700, with 65 per cent polymorphonuclear leukocytes, 4 per cent monocytes and 33 per cent lymphocytes. Urine on April 23, 1943, showed a specific gravity of 1.020, no albumin or sugar; microscopic, loaded with white blood cells. On April 5, 1943, specific gravity was 1.020, albumin +, sugar 0; microscopic examination revealed many red blood cells and occasional pus cells. Sulfathiazole crystals were present. The blood Kline and Kolmer were negative on three occasions. Blood cultures on March 29, 1943, and May 6, 1943 were reported negative. Blood agglutinations for E. typhi, paratyphi A and B, Brucella mellitensis and abortus and Pasturella tularensis were negative. Cerebrospinal fluid on May 6, 1943, showed a pressure of 65 mm.; grossly it was reddish and cloudy and contained many red blood cells and lymphocytes. Pandy test was negative, glucose was 57 mg. per cent and chlorides were 673 mg. per cent. Electrocardiogram on May 7, 1943, showed rapid sinus tachycardia. Chest plate on May 3, 1943, showed enlargement of the cardiac shadow with generalized enlargement of all the chambers. Slight passive congestion of the lungs was also present.

Clinical Course: The patient ran an irregular temperature curve with daily elevations to above 104° F. which on some days remitted to normal or nearly normal levels. Pulse rate was markedly elevated reaching 168 terminally. The patient was put on sulfathiazole after admission but this was discontinued on April 25, 1943. On April 3, 1943, the right eardrum showed obliteration of the markings. The heart appeared large on this day and there was gallop rhythm with a split first sound. There was dullness of the left base of the lung posteriorly with absent breath sounds over this area. The liver was palpated two fingers below the costal margin. On May 6, 1943, the blood showed no sickling. On May 8, 1943, she was given 500 c.c. of whole blood and her condition appeared very poor. On May 8, 1943, the patient was dyspneic and the pulse rate was 180. There were moist, bubbling rales throughout the chest. She was given ouabain 1/128 grain intravenously. Oxygen therapy was administered. On May 9, 1943, the blood pressure was 100/82. She appeared profoundly toxic and stuporous. The heart rate was very rapid. The breath sounds were almost entirely absent in the left base. On May 10, 1943, her condition was very poor, pulse weak and heart rate was 170. She died on May 11, 1943.

Clinical Diagnosis: Septicemia.

Dr. Edgar Hull: It has been my experience that whenever we fail to make a correct clinical diagnosis we fail for one of three reasons. First, we may not have sufficient information; second, the information which we have may not be accurate; and third, which is perhaps the most common reason for missing the diagnosis, we do not know enough. In order to minimize the role of insufficient information I would like to ask Dr. Bennett a few questions so as to clear up certain points in the clinical history.

Was the swelling slight or marked? The reason I ask this is because the swelling is pretty hard to fit in with other findings.

Dr. Granville Bennett: It was apparently quite marked. It was one of the first things the patient complained of.

Dr. Hull: Did the patient vomit incessantly or only once or twice?

Dr. Bennett: From the history I would say that the patient vomited only a few times.

Dr. Hull: That question is pertinent because of the suspicion of central nervous disease symptoms in this patient. I wonder if Dr. Bennett can say what is meant by the mucous patches?

Dr. Bennett: The lesion was not fully described in the record.

Dr. Hull: In that case we may be justified in assuming the lesions were similar to the bullous lesions present on the skin.

Dr. Bennett: I believe that is correct.

Dr. Hull: Another point I am interested in is the source of the vaginal discharge. Was it cervical or vaginal merely? I ask that question because it is recorded that the cervix moved with difficulty and that there was a mass in the left side of the pelvis.

Dr. Bennett: That question can not be very well answered from the case record. It is stated that the vaginal examination revealed a reddened cervix but the source of the exudate is not given.

Dr. Hull: Were bacterial studies done of the vaginal discharge, or urine or spinal fluid?

Dr. Bennett: I am sorry that I can not answer that question. It is my understanding that all the bacteriologic studies that were made were negative.

Dr. Hull: The patient's blood pressure is recorded a couple of days before she died. What was it on admission?

Dr. Bennett: The blood pressure is not recorded in the report of the orginal physical examination.

Dr. Hull: Another question I consider important relates to the cerebrospinal fluid pressure. It is reported as 65 mm. Was the pressure expressed as mercury or water?

Dr. Bennett: Water.

Dr. Hull: Was the fluid centrifuged, and if so, was the supernatant fluid clear?

Dr. Bennett: It was clear after centrifugation.

Dr. Hull: The blood in the fluid was then probably due to trauma of tap. Was a cell count done to determine the number of lymphocytes?

Dr. Bennett: It is listed as 6,000 cells.

Dr. Hull: Was there any history of this patient's having taken drugs prior to the appearance of the rash?

Dr. Bennett: There is no mention of that in the history.

Dr. Hull: After these preliminary questions we will review the symtoms which the patient had on admission. She was ill six weeks. Her illness began with crying, irritability and nervous manifestations. Shortly thereafter her feet and face and arms began to swell. This swelling subsided after two weeks. A few days before admission she developed skin lesions and later began to vomit. During this time she had fever.

Upon admission the following signs were present: She was acutely ill; she was irrational and had high fever. Scaly skin lesions and eczematous lesions on the left ear were noted and there were lesions of the mucous membranes of the mouth. There was vaginal discharge, the cervix uteri was not easily movable and there was a mass in the pelvis. Objectively the lungs and heart and central nervous system were negative at the time of admission. There was slight anemia, moderate leukocytosis and pyuria.

She later developed marked tachycardia, cardiac enlargement, gallop rhythm and other signs of congestive heart failure, and signs which might be attributed to left pleural effusion. Anemia became more severe and there was slight leukopenia. It is noted that markings of the left ear drum were obliterated.

Spinal fluid was found to be bloody with lymphocytes but normal chemistry.

The early pyuria was replaced with hematuria. Finally, it is noted, death occurred after an illness of two months.

In this case as in any other case in a conference of this kind, I think we should attempt to establish three points about the diagnosis: first, etiology and pathogenesis; second, site and nature of the lesions; and third, the functional disturbances and a prediction as to the cause of death.

The following are the thoughts we might have regarding the data available on admission of this patient as regards the etiology. I think most of us will agree that the etiology here seems to be infectious and the nature of the lesions inflammatory. Also there are no specific infectious diseases particularly suggested by the history; by this I mean specific infectious diseases characterized by skin lesions as well as systemic manifestations such as syphilis or disseminated lupus. Since from those data available on admission none of these seem to be suggested, it would seem therefore that the patient was suffering with sepsis from one of the pyogenic organisms, possibly a coccus.

In regard to the pathogenesis of the lesion: If this patient had pyogenic sepsis there had to be some site of entry. The possible sites of entry suggested are first, the skin. The skin lesions, however, are definitely stated to have appeared after the onset of the fever and the nervous manifestations, so if this patient had pyogenic sep-

sis it is more likely that the skin lesions were metastatic rather than the site of entry. Another possible site is the eczematous lesion of the left ear. The third possible site is the pelvic organs, which seem more likely since the cervix was reddened and there was discharge; the cervix was fixed and there seemed to be a pelvic mass. It is in the realm of possibility that this patient could have had a septic abortion which was concealed from friends, relatives, and even from the doctor. Another possible site of entry is the kidneys. In view of the pyuria with absence of other symptoms referable to the kidneys, I would believe that the pyuria was a manifestation rather than the source of the sepsis.

The sites of involvement definitely indicated by the data on admission are few. There was definite evidence of involvement of the skin. If the pus in the urine came from the kidneys and not from the vaginal discharge we could say there was evidence of kidney involvement. There was no definite involvement of the brain or heart, lungs or other viscera from the data.

Later developments, however, might give us additional reflections as follows:

Continuing on the supposition of pyogenic sepsis, there develops another possible site of entry, the ear, since it is recorded that the markings of the ear drum were obliterated.

We have evidence of further sites of involvement, for example, the kidneys; this time albuminuria and hematuria replacing pyuria. If the patient had sepsis this hematuria indicates acute nephritis or bleeding pyemic abscess in the kidney. It is recorded on the urinalysis report that sulfathiazole crystals were present in the urine; these could have caused hematuria.

Now, the heart: The heart in the later course of illness became markedly enlarged. If this is a case of pyogenic sepsis the cardiac enlargement and cardiac failure might be attributed to interstitial myocarditis and small abscess of the myocardium or perhaps a degenerative type of myocardial lesion.

Central nervous system: Apparently there were no objective signs of central nervous system disease except stupor and lethargy and irrationality which could be due to toxemia. The spinal fluid pressure was normal. The chances are that the blood was due to trauma of the tap. If this patient did have cerebral lesions on the basis of pyogenic sepsis there is the possibility that there could have been a cerebral abscess in a silent area, as for example the temporal lobe.

There was also evidence of involvement of the respiratory system; signs which could be due to pleural effusion were present. If there was respiratory involvement in pyogenic sepsis it is possible to have small or medium size abscesses with effusion or empyema.

The liver which previously was not palpable became enlarged; this can be attributed to passive congestion resulting from cardiac failure.

It seems quite obvious that the actual cause of this patient's death was heart failure and toxemia. In view of the later developments in the case, after admission, it might be in order to make a few further reflections on the etiology and pathogenesis although I believe that the patient's story fits in pretty well with pyogenic sepsis with unknown organisms.

We should consider one disease in which there occurs skin involvement together with visceral lesions—disseminated lupus erythematosus. The clinical picture in this case is not typical for disseminated lupus but I think it can be pointed out that it is not at all incompatible. In this disease the lesions are usually not bullous but may be. This patient's lesions were bullous. High fever is quite characteristic. This patient had high fever. Pleural effusion is common; this patient may have had pleural effusion. Leukopenia is characteristic; this patient had leukopenia on one of the two blood counts recorded. If this patient actually bled into the subarachnoid space, which seems unlikely, it should be noted that in disseminated lupus there may occur spontaneous bleeding due to thrombocytopenia. Moderate anemia, which this patient

developed, is the rule in disseminated lupus. Death within two months of onset is extremely uncommon, however; there are usually erythematous lesions. Heart failure is not characteristic, though cardiac enlargement is common. Pericarditis develops frequently. Endocarditis is quite frequent in disseminated lupus, described by Libman and Sachs. In this case there is no evidence of pericardial or endocardial lesions, though the latter may occur without murmurs. Arthritic manifestations which occur frequently in disseminated lupus were not present in this patient. There were no joint pains that I know of.

Therefore, I would say that the weight of the evidence indicates that this patient probably did not have disseminated lupus erythematosis.

I therefore am inclined to believe that the best bet, from the information available, is a diagnosis of sepsis from some pyogenic organism, entrance site unknown; perhaps the pelvis and possibly the middle ear, the organism from this unknown site entering into the blood stream causing metastatic lesions of the skin, of the kidneys, of the heart, possibly of the lung and pleura and possibly also of the brain, although we have no definite evidence of involvement of the brain. In the kidneys, if this diagnosis is correct, we would expect to find one or several abscesses, perhaps also diffuse nephritis; in the heart, interstitial myocarditis, perhaps with small abscesses. If lung involvement we might find abscesses with empyema in the left side. If brain involvement, perhaps abscess might be present in some relatively silent region.

Dr. Bennett: I would like to ask Dr. Hull why he dismisses the reported negative culture studies in arriving at his diagnosis?

Dr. Hull: I do not dismiss them but I certainly think that we can have septicemia and particularly pyemia, with repeatedly negative blood cultures. We often have difficulty in getting positive blood cultures even in cases of bacterial endocarditis. The blood culture is of more positive than negative value.

Dr. Bennett: This patient presented, at postmortem, findings that cause the pathologist to lean upon the clinician for support in submitting his interpretation. For that reason I think this is a particularly good case for a clinico-pathologic conference. It demonstrates clearly that the pathologist does not always have the last word.

I would like to state briefly the postmortem findings and then present, with the aid of lantern slides, our microscopic observations and discuss the disease process which we believe to be represented by this case.

The body of this patient was fairly well developed but undernourished. I think the undernourishment was compatible with the duration of the illness. She had a skin eruption that was represented at the time of postmortem by a dry scaly rash. The rash was more pronounced over the upper extremities and thorax, particularly on the anterior surface of the body. This rash (which was not fully or clearly described in the clinical record) was a rather dry silvery scaly type of lesion. There were no inflamed margins around any of the lesions.

On opening the body cavity, there was a pleural effusion on the left side measuring approximately 200 c.c. This consisted of a clear straw colored liquid. In some places a scant amount of fibrin was deposited upon the pleural surfaces. The pericardial cavity contained 25 c.c. of clear amber fluid. The pericardium was roughened, rather acutely congested and presented a dry granular surface interpreted as an early stage of inflammatory exudation. The lungs were both heavier than normal, weighing 380 grams each. The entire lower lobe of the left lung was consolidated. The findings were interpreted as indicating a confluent bronchial pneumonia. Other portions of the left lung and the right lung showed patches of consolidation and acute pulmonary edema.

The liver was slightly enlarged, appearing a short distance below the costal margin. The spleen was not remarkable on gross examination. The combined weight

of the kidneys was greater than normal. The left kidney weighed 140 grams. The kidneys were soft and pale and when sectioned the parenchyma bulged over the capsule.

There was no inflammatory mass in the pelvic cavity. We were unable to demonstrate any lesions that would explain the clinical findings described in the record. Other findings of importance were limited to the heart.

The heart was slightly enlarged, moderately dilated, and a little softened. When opened the most conspicuous lesion was found on the mitral valve. I think you can perhaps make out in this gross photograph the row of small vegetations just along the line of contact closure. At the time of postmortem the question was asked whether these were rheumatic vegetations. One must admit that they are consistent with the endocardial lesions of rheumatic fever. However, there was no suggestion of any involvement of the posterior wall of the left auricle such as is usually seen in rheumatic endocarditis with valve involvement of this degree.

This photograph will orient us with regard to the gross pathology in the lungs and kidneys. This is the left lung showing diffuse consolidation. The kidney shows a somewhat widened and thickened cortex with greater striation than one normally sees.

How were these gross autopsy findings to be interpreted? It seemed that the most important and significant lesion from a diagnostic point of view were the changes in the heart. We therefore delayed our summarization of the case in the hope that the microscopic sections might help us. I would like, at this time, to show the microscopic changes. We believe that these lesions are compatible with the disease process which Dr. Hull suggested as his second choice; namely, disseminated lupus erythematosis. This is a photograph of a section taken from the left lung. The section shows bronchopneumonia. In this region there is some interstitial infiltration. In the remainder of the lung there was a much greater amount of acute edematous exudation than is to be seen in this reproduction. This is one of the lesions that were seen on the mitral valve. This is the valve stroma on this side. Unfortunately it does not show very well on the screen but you can see that there is separation of the connective tissue stroma; a change that is referred to as "fibrinoid degeneration." This change is seen in disseminated lupus throughout the connective tissues of the body. Superimposed upon this "fibrinoid" lesion is a large thrombotic mass. Such vegetations contained no visible bacteria in specially prepared sections. Here at the base of the mass are numerous fibroblasts showing that the lesions are beginning to organize.

This photograph shows a similar vegetative lesion on the tricuspid valve.

I thought it might be of some interest to this group to present, in contrast to these vegetations, some photographs of the highly characteristic rheumatic fever lesions. This is small vegetation on valve of a heart affected by rheumatic fever. In lupus one sees "fibroid" degeneration. However, one does not see cellular responses of this type. This lesion is highly characteristic of active rheumatic fever.

Here is another rheumatic fever lesion; in this instance there is infiltration and vascularization of the valve. Here is an endocardial lesion. None of these lesions were found in the case discussed. The maximal cardiac change in the case presented tonight was fibroid degeneration in connective tissues.

One of the manifestations of lupus that is often regarded as being characteristic is the kidney lesions. These kidneys show rather less than we would have expected from the gross examination. There is swelling of tubules, and some vacuolization of the tubular cells. There are no hyaline or granular casts. Scattered throughout the kidneys were glomerular lesions of this sort. There is hyalinization of the capillary tufts and some adherence of the capillaries to the capsule. These lesions while not pathognomonic of this syndrome of disseminated lupus, are consistent with it. The

short duration of the disease process, in the present case, may have been a factor of importance in determining the extent of the renal changes.

In the spleen there were occasional vessels showing changes of this sort in the arterial walls accompanied by thrombosis and associated with necrotic foci. There were also larger vessels showing increased connective tissue in the adventitia. These changes have been described as typical of lupus or frequently associated with it.

Dr. Hull was impressed with the fact that there was no arthritis. It is perfectly true, according to the case record, that the patient did not complain of joint symptoms. We have observed in numerous cases that joint symptoms may be overlooked in seriously ill and bedridden patients. It is not uncommon upon routine examination of the joints to find foci of metastatic infection in the synovia in patients dead of pneumonia or other infectious diseases. In this patient the knee joint contained an excess quantity of synovial fluid. On the synovial surface there is fibrinoid material. The synovial villi are hypertrophied. There is also a moderate degree of cellular infiltration. I am sure that the fluid from this joint would have shown a marked increase in the number of cells.

The lesions of the skin, as shown in this photograph, are entirely consistent with those of disseminated lupus. The skin is much more corrugated than normal. The ducts are plugged with large scaly crusts of keratinized epithelium and this is a mild inflammatory reaction.

These are the anatomic findings in this case. I believe that from the morphology this case fits best with the syndrome that is referred to as acute disseminated lupus erythematosis. To a pathologist this diagnosis is an unsatisfactory one because the observed lesions exhibit extreme variation in severity and distribution. For instance some reports show that the kidneys are affected in 75 or 80 per cent of cases whereas, in other groups, kidney changes have been found in less than 50 per cent of the patients.

In the patient presented tonight there are lesions in the skin, kidney, heart, serous surfaces and vascular structures throughout the body which I believe can be interpreted as those of acute disseminated lupus erythematosis.

Dr. W. H. Harris: I did not expect that the president would call first upon pathologists for remarks concerning this interesting conference. I really feel that the clinicians should first present their comments in connection with the case that Drs. Hull and Bennett have discussed. However, after viewing the lantern slides of Dr. Bennett, I certainly concur in his pathologic interpretation. It does occur to me that more extensive and indicative lesions were curtailed by the comparative brevity of the primary illness. This latter was due to the superimposed acute pneumonic process which occasioned the patient's death. In looking at the pictures of the lung, while evidence of passive congestion is noted, there also occurred an acute exudative pneumonitis as evidenced in both the alveoli and the bronchial tubes.

It occurs to me that the clinical investigation of the case was somewhat inadequate. Dr. Hull had to ask many questions which should have been more specifically and clearly represented in the case history. Many such questions could not be answered as the information was not available. I was particularly impressed by the lack of replete gynecologic presentation. There was a definite abnormality reported for the vaginal examination. No progress report of the tumor mass and partial fixation of cervix was described. Likewise there was an apparent absence of bacteriologic investigation.

I believe this innovation into our Parish Society is a splendid one and I think that the audience as a whole should not hesitate to express their opinions and to ask questions which will enliven the interest and yield additional information. From this latter standpoint, I would like to ask Dr. Menville's opinion of the x-ray of the chest relative to lung and heart lesions.

Dr. Leon J. Menville: I do not recall

seeing this roentgenogram before. However, one should be very cautious in making an interpretation of pericarditis with effusion with what is seen on a flat film. The patient should be fluoroscoped for consideration of absence or diminshed pulsations, before one considers making a probable diagnosis of pericarditis with effusion. I believe, from that film alone, that you were dealing with a large heart.

Dr. Bennett: The heart weighed 250 grams. It was dilated and somewhat soft.

Dr. Randolph Lyons: I do not think it is fair for clinicians to get up with clinical and pathologic information and criticize Dr. Hull's discussion. He gave all of the symptoms of lupus which fit in perfectly and I do not see why he did not put this diagnosis first.

Dr. Edwin H. Lawson: Since this case has been so thoroughly presented by both Dr. Hull and Dr. Bennett and as I have never personally seen a case of this type, it would be facetious for me to attempt a discussion. I would like to ask Dr. Bennett for an explanation of the pelvic symptoms and what, if any, were the changes in the liver.

Dr. C. J. Tripoli: It was really a treat to listen to the speakers giving their most interesting discussion of this case.

There are only two questions in my mind: What, if any, cultures were made of the heart blood at autopsy? What, if any, arterial changes were found in the pulmonary circulation?

Dr. George Hauser: I would like to ask what the examination of the nervous system disclosed?

Dr. W. A. Wagner: I would like to know why, in view of the fact that the clinical history signified trouble with the ear, was it not autopsied and in view of the bacteriologic phase of the case, anaerobic cultures were not made. Infection may have been in the lateral sinus or ear and since the etiology of this case is not known such a study might have disclosed an etiologic factor.

Dr. Bennett: In answer to the questions asked by Dr. Lawson: There were no specific changes in the liver; only slight to moderate congestion. There were no lesions in the pelvis to explain the physical findings or the symptomatology suggesting an inflammatory disease. The peritoneum was smooth and uninvolved, although in lupus it is not uncommon to find serious surface changes affecting pelvic organs.

Someone inquired about cultures of the heart blood. Cultures taken at the time of postmortem were negative.

There were no specific changes observed in the pulmonary arteries which could be considered specific in any way.

The central nervous system was not examined because permission for such examination was not granted. Since this case showed some of the signs of central nervous system involvement that are not infrequently noted in lupus, it is unfortunate that the brain was not studied. While the pathologic changes associated with central nervous system involvement have not been completely worked out, it is probable that vascular lesions such as those found in other parts of the body, are responsible for the central nervous system symptoms.

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THE LOUISIANA STATE UNIVERSITY MEDICAL SCHOOL

It is with very real dismay that we have been reading in the pages of the local New Orleans papers of the difficulties at the Louisiana State University Medical School. These troubles seem as if they have been magnified considerably by the papers and what might at the onset have been handled quietly and tactfully, has finally stirred up a great deal of really unnecessary feeling. Certainly at the start of the controversy a tactful attitude by those concerned might have alleviated the disagreeable conditions that have now arisen.

A situation such as this is tragic. It is impossible for the average teacher of medicine who is on a full time basis to get up and go to another medical school when and if he so feels like it. It is very difficult for a full time man to teach in an atmosphere which is not conducive to an academic spirit, and to carry on research and investigative problems when there is a feeling of uncertainty and unrest. The undergraduate students are to be commiserated with because there is no doubt but that their medical education will be in a sense injured or hurt by the feeling of unhappiness that now exists among these boys as well as among their teachers.

It is earnestly hoped that by the time this editorial is published that the difficulties that the school is now having will have become dissipated and will be gone. The Louisiana State University Medical School, started under difficulties, has become one of the outstanding medical schools of the South. It is our sincere wish that it will maintain the high standards that it has upheld in the past few years.

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DR. FRANCIS FENWICK YOUNG

It was with sincere regret and the sense of a great loss that the medical profession, especially the organized medical profession of the State of Louisiana, learned of the death of Dr. Francis Fenwick Young of Covington, La., September 26, 1945. A brief biographic sketch of this pioneer psychiatrist will demonstrate the unusual abilities and qualifications of this accomplished physician.

Dr. Young was born in Abbeville, La., on July 30, 1863, the son of a physician, Dr. Francis Devillier Young and Marie Mathilde Guegnon. He was graduated

from St. Charles College, Grand Coteau, La. on July 25, 1881, with a B. S. degree, and received his M. D. degree from the University of Louisiana (now Tulane) in 1884. For one year he interned at the Charity Hospital, New Orleans. In 1892 he founded the Fenwick Sanitarium at Abbeville, La., and remained the Director and Psychiatrist-in-Chief of this institution bearing his middle name until his death. He moved to Covington, La. in 1912 and continued his sanitarium in this new location, feeling that the climate and location were better suited. He held diplomas for post-graduate work at Columbia University, New York Post-Graduate School, New York Polyclinic and other Eastern schools. A member of organized medicine and many medical societies, he was always active in such work. He was an honorary member of Alpha Kappa Kappa Fraternity from the chapter at the University of Texas.

A pioneer in his field, he was the first physician to report cases of beriberi in Louisiana, in 1903. This article was published in the Journal of the American Medical Association in January of that year. His opinions concerning the problems of the alcoholic and drug patient, new in concept at that time, proved to be correct and became commonly accepted. He published many other valuable articles.

Dr. Young's was a family of physicians. In addition to his father he had five brothers and four sons who practiced medicine, two of them surviving to carry on the valuable work of the Fenwick Sanitarium he established.

The family of Dr. Young have a valuable heritage and the surviving four sons a reputation to maintain.

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PREOPERATIVE USE OF THIOURACIL IN HYPERTHYROIDISM

Since its introduction into modern therapeutics, much has been written concerning the drug thiouracil. The evaluation of its usefulness in the preoperative treatment of severe hyperthyroidism by Lahey, Bartels, Warren, and Meissner* is timely and interesting.

The clinical observations upon which this report is based cover a period since May 1943. It was felt that the drug had been proved to be capable of reducing an elevated basal metabolic rate of hyperthyroidism to normal if administered over a long enough period of time and that there was a gradual disappearance of symptoms except the eye symptoms if these were pronounced. It was not felt that there was any proof that permanent remissions in hyperthyroidism could be secured by administration and then withdrawal. That it was valuable in the preoperative management of hyperthyroidism seemed conclusive.

The authors' experience covers 190 patients with severe hyperthyroidism treated preoperatively with thiouracil, followed by thyroidectomy. Both Graves' disease and toxic adenomatous goiter were included. No case failed to respond to the drug. Early in their experience they found that with the use of the drug two-stage thyroidectomies could be eliminated and so-called thyroid storms postoperatively avoided entirely. However, in mild hyperthyroidism preparation with iodine was still recommended since sufficient remission could be secured preoperatively without the risks involved in the use of thiouracil.

In most cases, surprisingly enough, the treatment was ambulatory. They were seen at regular intervals for examination and white and differential blood counts were made, usually every 10 to 14 days. The dosage was a total of 0.6 gram daily, 0.2 gram at 7 a. m., 2 p. m., and 9 p. m. until the desired result was obtained.

An interesting observation was the increased friability of the gland at operation with extensive bleeding of the entire operative site. It was then found that when Lugol's solution was administered

*Lahey, Frank H., Bartels, Elmer C., Warren, Shields, and Meissner, William A.: Surg., Gyn., and Obstet., 81:425-439, 1945.

during the three weeks' period before operation the friability of the gland was overcome. Iodine and thiouracil were given simultaneously for two weeks and then for one week preoperatively only iodine was given. It was believed that involution of the gland is furthered when thiouracil is not being administered. Those patients who received Lugol's solution before thiouracil was begun responded less quickly and usually required a longer period of treatment. Of the 190 cases there were no postoperative deaths.

Toxic manifestations occurred in 23 of the 196 patients given thiouracil. Leukopenia and granulocytopenia were the most frequent and most alarming reactions, including fever, skin eruption, scleredema, and swelling of the salivary glands.

ORGANIZATION SECTION

The Executive Committee dedicates this page to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.

An informed profession should be a wise one.

CONFERENCE ON MEDICAL SERVICE AND PUBLIC RELATIONS

There was held in Chicago on October 19 and 20 a conference of the Council on Medical Service and Public Relations of the American Medical Association. Two representatives from every State Medical Society were invited to attend this conference. There was representation from the Louisiana State Medical Society and a review of the transactions and some of the highlights of the important subjects discussed should prove of interest.

It was brought out that the Wagner-Murray-Dingell Bills (S. 1050 and H. R. 3293) are still in committee and there appears to be at present very little activity among the congressmen in regard to having this important measure given a hearing before the committee. However, it was very evident that much attention was being given to other bills, such as the Hill-Burton Bill (S. 191) and the EMIC Bill (S. 1318). These measures appear to be, from reliable information, substitute measures, similar provisions of which occur in the master bill S. 1050. Hearings have recently been conducted on S. 191 which provides for a survey of hospitals and expansion of hospital facilities in the United States on a state level. There has been a widespread support of this measure by medical and hospital groups; however, there has not yet been any report given out from the committee. The present status of the EMIC Bill is stationary. There has been no hearing due to the fact that Senator Pepper is out of this country making some observations in Europe. On the whole, the outlook for any decision on these vital measures in the near future is rather remote. Obviously it is imperative that each and every physician of this state continue to use whatever pressure and influence he can on his congressmen to oppose such legislation.

The tendency of the congressmen seems to be away from any new bills creating additional taxes as the feeling now is obviously to reduce taxes.

There is a great deal of interest manifested in several bills looking toward the creation of a Scientific Research Bureau under control and supervision of the federal government. We should all remember and should call attention to the fact when talking to our congressmen, that there should be a distinction made between the results of

scientific research and their application for the good of the people. This application should not be left to federal control but should be given out to the various groups and agencies for proper dissemination and use for the citizens of this country.

There was considerable discussion at the conference in reference to voluntary prepayment medical insurance plans. In regard to the various plans—their failures and successes—there were no particular new thoughts brought out. However, in the discussion it was demonstrated that a great many of these insurance projects had failed due to lack of uniformity over the whole country. There were very strong arguments brought forward that this form of medical insurance should be of a national scope, having a uniform policy. This then could be altered or changed as the insurance laws of the respective states demanded. Obviously this is intended to meet the growing demand on the part of the industrial businesses of the country to have a coverage for all of their employees in all states in which they are employed. For example, the American Telephone and Telegraph Company, Western Union, various automobile industries, packing houses and other big corporations that prefer such a plan for their employees. This would prevent the necessity of carrying a different policy in every state where the industry may have branches. Many of these companies are postponing adopting this form of insurance for this reason and it has been recommended to the Board of Trustees of the A. M. A. that some form of a national health agency for prepayment medical insurance be sponsored by the A. M. A.

The lack of uniformity exists also in the Blue Cross insurance where a plan for the entire country is now being discussed. It seemed that there was considerable approval of this plan by the representatives present at the conference with the hope that the past jealousy between the Blue Cross plan and medical service plans would be abrogated. The feeling also existed that our medical organizations have been more or less on the defensive side in regard to furnishing adequate medical care to needed areas and have not offered a constructive plan in this regard. This question approached such an issue that there appeared on the program a gentleman representing an insurance company, offering to sell same to the A. M. A. if this is desired.

There is an organization already formed, known as the American Medical Insurance Company, in New York, which is preparing to write a policy for a national program of medical service. This may be a solution to the problem. It is interesting to know that the American Association of Industrial Physicians and Surgeons is behind the program.

It was reported from Brooklyn that a group of physicians there is fostering a national plan for medical service. Also the Medical Society of New York recently, through their House of Delegates, relegated to the Council the right to go ahead with a program, the details to be worked out later. This is to be a casualty company, nonprofit, chartered under the laws of New York.

The various state societies have been asked to support a national plan. What may come from these constructive suggestions is of course doubtful; however, it is thought that these facts would prove of interest to our members.

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TERMINATION OF HEALTH PROJECTS UNDERTAKEN AS WAR MEASURES

At the invitation of the Director of the State Board of Health a special committee, from the Executive Committee, met with the Board on October 11. The subject matter discussed was the position of the Executive Committee of the State Society in regard to continuation of the venereal disease clinic at Delgado Memorial. The meeting was opened by explanatory remarks by the President of the Board of Health after which the members of the special committee presented the attitude of the Executive Committee in desiring that the clinic be discontinued. The committee also answered questions from various members

of the Board as to the ability of the medical profession to take over this work after it is discontinued by the Board of Health.

While not on the agenda for discussion, the question of extending the EMIC program was also discussed and the members of the group presented to the Board the reasons for the medical profession's desire to discontinue this service in accordance with agreement in 1943.

The committee was received very cordially and hospitably and Dr. Brown. for the Board, expressed thanks for such cooperation on behalf of the Executive Committee of the State Society. He stated he wished to assure the State Society that the Board is most desirous of cooperating and accepting the wishes of the medical profession in these vital matters.

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LOUISIANA STATE MEDICAL SOCIETY NEWS

CALENDAR

PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of very month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

CORRESPONDENCE

Below is copy of letter received by the Secretary-Treasurer from Commander Shirley C. Lyons.

Samar, Philippines,

August 30, 1945.

Dear Paul:

From time to time I receive short notices from the State Medical Society bearing your signature. I want to assure you that any news from home concerning medical society activities is always most welcome. The most recent news with your name was a reprint from the New Orleans Medical and Surgical Journal "Postwar Medical Planning". I answered a questionnaire from that committee some time ago. I do not have a copy of the answer and am wondering if my views have changed. The younger men all seem to be interested in further training and wish a residency in some special work. A fair number will need ordinary internships. The older group, as yours truly, will want about three months to do as we please and will probably spend part of the time attending clinics. (At least that will be a good excuse). No matter how we spend the time it will require about three months for a period of readjustment after we have been discharged from the service. We have worked hard (at least most of us have) contrary to the general idea that most of the folks back home seem to have developed regarding medical men in the service. We are all proud of the fact that we had an opportunity to serve the armed forces. We all realize that each of you at home did just as much and made just as many sacrifices. We are all tired of the military life and anxious to get home. This of course, is especially evident now since the fighting is over. In this particular area it looks as if we will be needed for a period of at least three more months, possibly longer. I am perfectly willing to remain here until our job is completed and then return to the States for complete separation from the service.

We have a 3500 bed hospital with all facilities right in the middle of the jungle. The duty is only semi-rugged. Up until peace was declared we were very busy and at the rate we were receiving patients we were already looking for more beds. We certainly had no idea the war was coming to such a rapid close. We had the survivors from the Indianapolis here and of course we were all terribly upset over that tragedy. I have seen enough injured men to last me the rest of my life.

We had a staff of 70 plus doctors (already losing them since peace). I enjoyed the title of Chief of Surgery. Our hospital census is around 1800 now and unless something unforeseen develops it should show a gradual decline. They have sufficient dispensaries out here to handle the routine work.

So far as I can judge at present I should be back with you by the next meeting of the State Society at least. I hope this finds all well with you. With very good wish.

Sincerely,
Shirley.

LAFOURCHE VALLEY MEDICAL SOCIETY

A reorganization meeting of the Lafourche Valley Medical Society was held in Thibodaux on Wednesday, October 3, 1945, at which time the following officers were elected: Dr. Guy R. Jones, President, Dr. H. L. Haydel, Vice-President, Dr. Philip Robichaux, Secretary-Treasurer.

BI-PARISH MEDICAL SOCIETY

The Bi-Parish Medical Society met at the East Louisiana State Hospital on October 3. After an excellent dinner, prepared by the institution, the society convened in the staff room for a scientific program.

Mr. M. A. Taff of the Vital Statistics Department of the State Board of Health addressed the meeting concerning reporting of birth by attendants and parents of children thereby raising the percentage of births reported. East Feliciana Parish is one of the parishes selected to initiate this system.

Dr. E. M. Robards discussed tuberculosis from x-ray interpretation of the lungs of a patient.

Both speakers were extended a vote of thanks for presentation of these subjects. A vote of thanks was also given Dr. Glenn J. Smith and Staff for the excellent entertainment and dinner given the society.

SOUTHERN BAPTIST HOSPITAL

A clinical staff meeting of the Southern Baptist Hospital was held on Tuesday, October 23 at 8 o'clock. Dr. R. O. Harris gave a case report of "Migraine Headaches Followed by Sudden Death." Dr. Howard Mahorner spoke on "Restoration of Continuity after Resection of the Rectum" which was followed by a motion picture on abdominoperineal resection for carcinoma of the rectum, one stage operation, by Dr. Thomas E. Jones of Cleveland Clinic. The last discussion was the death report by Dr. Philip Tiller.

OCHSNER CLINIC

A meeting of the Ochsner Clinic staff members and Fellows was held on Friday, October 26 at 8:30 p. m. in the reception room of the Clinic. The following program was presented: Colonel Mims Gage spoke on "The Care of Paraplegics"; Dr. George Burch spoke on "Demonstration of New Plethysmograph for the Study of Peripheral Blood Vessels" and Dr. Dean Echols discussed "Herniation of the Temporal Lobe into the Cerebellar Fossa."

NEWS ITEM

The generosity of the Henderson family towards Tulane is further exemplified by the announcement by President Harris of a bequest by Miss Sarah Henderson of $1,075,000 for the endowment of the Chair of Tropical Medicine and for the improvements and changes in that Department. The receipt of this gift will further enhance the resources of the Department of Tropical Medicine so that it may become ultimately, as it is hoped, the outstanding Department in any American University Medical School.

Dr. Samuel B. Nadler attended a round table discussion of the Seventh District Medical Society in Rayne, Louisiana on Thursday, October 4. The title of Dr. Nadler's talk was "Headache."

Dr. William B. Clark, professor of ophthalmology, Tulane University, has just returned from Yepocapa, Guatemala, where he spent six weeks instituting a research project in the cause of blindness in patients infected with onchocerciasis in Guatemala. This project is sponsored jointly by the Caribbean sector of the Pan American Sanitary Bureau and the Department of Health of Guatemala. The project is being continued in Dr. Clark's absence, by Dr. Bertha Riveroll Noble of Mexico City, D. F., who was a former Pan American Kellogg Foundation fellow in ophthalmology at Tulane University from 1943 to 1945. Dr. Clark will return to Guatemala in January, 1946, to close out or continue the project as the results of the investigation justify.

Smith, Kline, and French Company has made a grant of $5000.00 to the Alton Ochsner Medical Foundation for research in chemistry, according to Dr. Thomas Findley, the Research Director of the Foundation. This fund will be used to continue the work on enzymes which is being done by Dr. Otto Schales, Director of the Chemical Research Laboratory.

SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE SOUTHERN SECTION

A meeting of the Society for Experimental Biology and Medicine was held on Friday, November 9 at 8:00 p. m., in the Richardson Memorial Building on the uptown Tulane campus. The following papers were presented:

1. Toxicity of Nicotinic Acid and Some of its Derivatives, by F. G. Brazda and R. A. Coulson, Department of Biochemistry, L. S. U. School of Medicine.

2. A Simple Method for the Determination of Glucose in Blood, by Otto Schales and Selma S. Schales, Chemical Research Laboratory of the Alton Ochsner Medical Foundation.

3. Reaction of Nerve to Restriction of Growth by Ligature, by D. Duncan (introduced by H. A. Davis), Department of Anatomy, L. S.U. School of Medicine.

4. The Effect of Experimental Arteriovenous Fistula on Circulation Time and Auricular Pressure in Dogs, by E. C. Heringman, H. A. Davis, and J. C. Rives, Department of Surgery, L. S. U. School of Medicine.

5. The Effect of Partial Hepatectomy Upon the Metabolism of Alpha-Estradiol, by Albert Segaloff, from the Alton Ochsner Medical Foundation and Department of Medicine, Tulane University School of Medicine.

6. In Vitro Susceptibility of Histoplasma Capsulatum, by John H. Seabury (introduced by H. A. Davis), Department of Medicine, L. S. U. School of Medicine.

7. (Read by title): Spinal Fluid Protein in the Retrospective Diagnosis of Subclinical Poliomyelitis, by W. B. Andelman, William I. Fishbein and A. E. Cases, Chicago Board of Health and the Birmingham Baptist Hospital.

A short business meeting was held at 7:45 p. m.

MILITARY PROMOTIONS

Information has been received that Raphael S. Hernandez, of Duson and Edwin S. Kagy, of New Orleans, have been promoted from Major to Lieutenant Colonel in the U. S. Army.

Major John C. Swartzwelder, Sn C., of New Orleans, has been assigned to Camp Shelby, Mississippi.

Captain James W. Vaudry, MC., of New Orleans, has been assigned to McCloskey General Hospital, Temple, Texas.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, INC.

The next written examination and review of case histories (Part I) for candidates will be held in various cities of the United States and Canada and by special arrangements at Army and Navy Stations on Saturday, February 2, 1946 at 2:00 P. M. Candidates who successfully complete Part I examination proceed automatically to the Part II examination held later in the year. All applications for this year's examinations must be in the office of the Secretary by November 1, 1945.

For further information and application blanks, address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh, 6, Pennsylvania.

INTERNATIONAL COLLEGE OF SURGEONS

The tenth annual convention of the International College of Surgeons will be held at the Mayflower Hotel, Washington, D. C., on December 7 and 8, 1945. A scientific program has been arranged for both days.

ASSISTANTSHIP DESIRED

A member of the State Society, recently discharged from military service, is desirous of securing an assistantship with a diplomate in either otolaryngology or ophthalmology or both. If interested in securing the services of such an assistant kindly communicate with the office of the Journal, 1430 Tulane Avenue, New Orleans, for further information.

SOUTHERN MEDICAL ASSOCIATION MEETING

At the meeting of the Southern Medical Association in Cincinnati, Ohio, November 12-15, 1945, the following Louisiana doctors were on the program.

Section on Medicine: Dr. G. A. Goldsmith gave the Chairman's Address which was entitled "Importance of Vitamins of the B Complex in Clinical Medicine." Drs. W. A. Sodeman and Vincent J. Derbes spoke on "The Febrile Asthmatic."

Section on Physical Medicine: Dr. Nathan H. Polmer delivered the Chairman's Address, the subject being "Simon Baruch, Father of American Hydrotherapy."

Section on Surgery: Dr. Robert A. Robinson spoke on "Surgical Complication of Amebiasis."

Section on Obstetrics: Dr. Woodard D. Beacham gave a paper on "Study of the Abdominal Pregnancy Cases Managed at the Charity Hospital at New Orleans, and a Review of the Literature."

Section on Anesthesiology: Dr. John Adriani gave the Chairman's Address on "Some Practical Aspects of the Chemistry and Pharmacology of Local Anesthetics." Dr. Ray T. Parmley gave a lantern slide demonstration of "The Use of Saddle Spinal in Obstetrical Analgesia."

At a meeting of the American Society of Tropical Medicine which met conjointly with the Southern Medical Association, Dr. Ernest Carroll Faust gave a talk on "The Diagnosis of Schistosomiasis Japonica, the Symptoms, Signs and Physical Findings Characteristic of Schistosomiasis Japonica in a Native Family on Mindanao, Philippine Islands."

INFECTIOUS DISEASES IN LOUISIANA

The weekly morbidity report for the State of Louisiana for the week ending September 1 contained information concerning number of venereal disease cases, listing 1,456 of gonorrhea, 774 of syphilis, and five cases of lymphopathia venereum. Other diseases reported in numbers larger than ten were as follows: 147 of cancer, 121 of unclassified pneumonia, 74 of pulmonary tuberculosis, 39 of chancroid, 24 of granuloma inguinale, 22 each of pneumococcic pneumonia and rheumatic fever, and 12 of endemic typhus fever. This

week there were seven cases of poliomyelitis reported; two in Caddo and two in Claiborne Parishes, one in St. Tammany and one in Bossier and one out of the state. Five cases of malaria were reported, one contracted within the continental U. S., two outside continental U. S., and place of contraction of two was not stated. There were more cases of influenza reported for the week ending September 8 than of any other disease; 139 cases listed. Other diseases included 19 of malaria, 18 of septic sore throat, 16 of pulmonary tuberculosis, 13 of scarlet fever and unclassified pneumonia, and 12 of endemic typhus fever. Of the malaria cases reported, eight were contracted within continental U. S., four outside of continental U. S., and place of contraction of seven was not stated. There was one case of meningococcus meningitis reported in Orleans Parish; one of pellagra in Calcasieu; four of poliomyelitis in Caddo and one of poliomyelitis in Calcasieu, Lincoln and St. Landry Parishes. For the week ending September 15 there were reported 38 cases of malaria, 35 of which were contracted within the continental U. S. The same number of cases of pulmonary tuberculosis were reported this week and also 30 of bacillary dysentery, 21 of septic sore throat, 14 of endemic typhus fever, 13 of diphtheria and 11 of influenza. One case of meningococcus meningitis was reported from both Orleans and Washington Parishes. The report for the week which terminated September 22 listed 55 cases of pulmonary tuberculosis, 34 of influenza, 20 of whooping cough, 16 of endemic typhus fever, 15 of diphtheria, 12 of scarlet fever and 10 of poliomyelitis; this last disease being reported, one case each, from seven parishes, two from one parish, and one from out of the state. There were five cases of undulant fever reported from Calcasieu Parish this week. The last report received which was for the week ending September 29, included the following diseases in numbers greater than ten: endemic typhus fever 29, influenza 26, septic sore throat 25, diphtheria and malaria 23 each, pulmonary tuberculosis 20, scarlet fever 16, and bacillary dysentery 13. Eighteen of the cases of malaria were contracted within continental U. S. One case of meningococcus meningitis and one case of poliomyelitis were reported from Jefferson Parish.

HEALTH IN NEW ORLEANS

The Bureau of the Census, Department of Commerce, reported that for the week which closed September 22 there were 121 deaths in the City of New Orleans, 79 of whom were white and 42 colored. Thirteen of these deaths occurred in individuals under one year of age; nine white and four colored. The next week, ending September 29, there were 126 deaths reported; 83 white and 43 colored, 15 of whom were in infants, divided almost equally between the two races. The report for the week which closed on October 6 showed a decrease in the number of deaths, there being only 103 listed this week. The deaths among the white population numbered 66 and the non-white 37. Only five infants expired this week; three white to two colored.

WOMAN'S AUXILIARY

Following are the officers of the Woman's Auxiliary to the Louisiana State Medical Society for 1945-46:

Officers

President—Mrs. Paul G. Lacroix, 3132 State Street Drive, New Orleans.

President-elect—Mrs. Arthur Long, 1367 Steele Drive, Baton Rouge.

First Vice-President—Mrs. Carroll Gelbke, 44 Willow Drive, Gretna.

Second Vice-President—Mrs. O. B. Owens, 1931 Military Highway, Pineville.

Third Vice-President—Mrs. B. C. Garrett, 4700 Fairfield Ave., Shreveport.

Fourth Vice-President—Mrs. A. G. McHenry, 1810 Riverside Drive, Monroe.

Treasurer—Mrs. Richard Vincent, 1441 Eleonore Street, New Orleans.

Recording Secretary—Mrs. Frank Jones, 810 Park Blvd., Baton Rouge.

Corresponding Secretary—Mrs. Willard Wirth, 402 Vincent Avenue, New Orleans.

Chairmen of Standing Committees

Archives—Mrs. Ansel Caine, 5301 St. Charles Avenue, New Orleans.

Bulletin—Mrs. Earl Clayton, Norco.

Cancer Control—Mrs. Herman B. Gessner, 119 Audubon Blvd., New Orleans.

Doctor's Day—Mrs. Geo. J. Taquino, 18 Fontainbleau Drive, New Orleans.

Finance—Mrs. Donovan C. Browne, 4920 St. Charles Ave., New Orleans.

Historian—Mrs. John S. Dunn, 8410 Pontchartrain Blvd., New Orleans.

Hygeia—Mrs. Leo. J. Kerne, Thibodaux.

Indigent Widow's Fund—Mrs. Aynaud Hebert, 2013 Napoleon Ave., New Orleans.

Legislation—Mrs. C. Grenes Cole, 4938 St. Charles Ave., New Orleans.

Organization—Mrs. Arthur Long, 1367 Steele Drive, Baton Rouge.

Parliamentarian—Mrs. A. A. Herold, 1116 Louisiana Ave., Shreveport.

Press and Publicity—Mrs. Roy Carl Young, Covington.

Printing—Mrs. Daniel J. Murphy, 127 South Solomon Street, New Orleans.

Program—Mrs. J. E. Heard, 512 McCormick Street, Shreveport.

Public Relations—Mrs. Rhodes Spedale, 701 Eden Street, Plaquemine.

Red Cross—Mrs. William Kohlmann, 1330 Eleonore Street, New Orleans.

Revision of By-Laws—Mrs. J. Kelly Stone, 72 Fontainbleau Drive, New Orleans.

War Participation—Mrs. Clarence Erickson, 423 Herndon Ave., Shreveport.

Councilors

First District—Mrs. Jules Myron Davidson, 100 Fontainbleau Drive, New Orleans.

Second District—Mrs. Roy B. Harrison, 2327 Napoleon Ave., New Orleans.

Third District—Mrs. Jules E. Dupuy, New Iberia.

Fourth District—Mrs. William J. Sandidge, 522 Stephenson Street, Shreveport.

Fifth District—Mrs. DeWitt T. Milam, 1704 Island Drive, Monroe.

Sixth District—Mrs. Marquis C. Wiginton, Hammond.

Seventh District—Mrs. Olin Moss, 2011 Shell Beach Drive, Lake Charles.

Eighth District—Mrs. Hiram O. Barker, Horseshoe Drive, Alexandria.

Advisory Board

Dr. W. R. Metz, Chairman, New Orleans; Dr. King Rand, Alexandria; Dr. Rhodes Spedale, Plaquemine.

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BOOK REVIEWS

Trauma in Internal Diseases; With Consideration of Experimental Pathology and Medicolegal Aspects: By Rudolf A. Stern, M. D. Foreword by Francis Carter Wood. New York, Grune & Stratton, 1945. Pp. 575. Price, $6.75.

This unusual condensed volume of 575 pages lives up to its title remarkably. Interestingly, it presents in a readable manner, amply illustrated by case reports, the medicolegal aspects of traumatic relationship to the entities encompassed by the internist.

To the reviewer it is remarkably educational. The author unfolds the controversial aspects of the laws governing compensation and further emphasizes the complicity of trauma as related to internal medicine since the relationship is so less obvious than in surgical disease.

Following the introduction are twenty chapters each of which covers a different aspect of internal medicine. The first chapter covers the infectious diseases and here the reviewer finds to his surprise a developed issue showing the possibilities of cause or spread of infection by any of three manners: creation of entry portal, traumatically rendered susceptible tissue permitting localization and trauma to previously infected tissue accentuating the pre-existant disease process.

The cardiologist finds his field amply covered in four chapters entitled: diseases of the heart, arterial diseases, diseases of the veins and essential hypertension. Remarkable completeness in relation to all cardiovascular entities is noted. In addition seven pages are devoted to aggravation of circulatory diseases by trauma.

The sixth chapter reviews pulmonary disease while the seventh chapter is devoted to entities involving the pleura. A supplement considers mediastinal involvement.

The gastroenterologist finds an elaborate nine chapters devoted to his specialty under the headings of esophageal, gastroduodenal, intestinal, appendiceal, peritoneal, hepatobiliary and pancreatic disease.

An elaborate 46-page section creates a relationship of renal diseases to trauma.

The traumatic genesis of malignant neoplasm is remarkably abbreviated into a six-page seventeenth chapter.

Defective metabolism and endocrinopathy, each enjoys adequate consideration.

The final chapter is devoted to hematologic and lymphatic disorders.

It becomes apparent from the above that all branches of internal medicine have their medicolegal aspects. Anyone can easily benefit from a review of this authoritative text. It will serve as an excellent reference as is illustrated in that the bibliography covers fifty-nine pages.

At this present time when many of us will be asked an opinion on disease entities concomitant, coincidental or resulting from defense industries and from actual combat duty it will serve us well to have the knowledge of this reference to protect our conclusions.

The author is to be complimented on the timely publication of a voluminous, authoritative study that should enjoy excellent reception by the profession.

GORDON MGHARDY, M. D.

Fundamentals of Pharmacology: By Clinton H. Thienes, M. D., Ph. D. New York, Paul B. Boeber, Inc. Pp. 497. Price, $5.75.

As expressed in the editor's preface, this is one of a series of textbooks designed for medical students in which no attempt has been made to treat the subject exhaustively. On the contrary it has been the object to include essential information on the subject within limits compatible with the time available to students involved in an expanded curriculum. In spite of this fact the scope of the book in comparison with other texts, has not been appreciably curtailed since in addition to consideration of the drugs in common use it includes sections on hormones, vitamins, pharmacy and prescription writing. Also an interesting and valuable innovation is the section on "Actions of Drugs on Cells" in which drug action is discussed from the standpoint of cellular structure and metabolism. Although this is a field of study still in its infancy it promises to assume increasing importance in pharmacology as knowledge of the normal structure and metabolism of the cell increases. Consequently, it is essential that the student have at least an introduction to this subject. The arrangement of material shows certain innovations such as the discussion of stimulants of the central nervous system as the first section. Special minerals are interspersed with the hormones in appropriate relationships, iodides following the thyroid, calcium following the parathyroids and iron in close association with the antianemic principles of liver and stomach. Uusually in the discussion of each drug emphasis is placed upon pharmacodynamics or action. In addition manifestations of toxicity and therapeutic uses are discussed briefly and official preparations with dosage are cited. As is common in first editions there are certain errors and mis-statements. Questionable statements may also be found. The latter are almost unavoidable in attempting to present all pertinent information with a minimum of discussion. The adequacy of this book will depend largely on the purpose for which it is used or on the demands which are made of a text. In it the student will find the essentials of pharmacology presented in a concise form sufficient for him to meet the requirements of his professor in medical school. He however will find it deficient if he wishes to use it as a source of information which would supplement or extend that acquired in his didactic courses.

RALPH G. SMITH, M. D.

A Textbook of Ophthalmology: By Sanford R. Gifford, M. A., M. D., F. A. C. S. 3d ed. rev. Philadelphia, W. B. Saunders Co., 1945. Pp. 457. Price $4.00.

This third edition is a fitting tribute to the memory of a truly great ophthalmologist. The table of contents has been amplified, the illustrations improved and the subject matter revised in an orderly and up-to-date manner. Illustrating the progressive trend of this volume is the emphasis placed on the frequence, importance and recognition of degenerative diseases in ophthalmology. The classification of retinal vascular scleroses is more complex and less complete than desirable.

Primarily intended for undergraduate instruction, revisions are including more material which adapts itself for simple, postgraduate teaching; such are the descriptions of the Maschek, Blascovics, and Dicky operations for ptosis. The author's encyclopedic knowledge of ophthalmology and wide clinical and teaching experience reflect themselves in the personality of this small volume of four hundred and fifty pages.

This book will probably become the outstanding textbook in its group partly because future revisions will be edited by Francis H. Adler, one of America's ace ophthalmologists and writers.

CHAS. A. BAHN, M. D.

Trichinosis: By Sylvester E. Gould, M. D., Springfield, Ill., Charles C. Thomas Co., 1945. Illus. Pp. 356. Price $5.00.

The 290 pages devoted to material in this 356 page book contain the complete story of this cosmopolitan disease. Only one thing is lacking which physicians are constantly seeking, namely the recommendation of an efficient form of treatment. This is certainly not the fault of the author, as all known methods of treatment are impartially reviewed.

Profusely illustrated with superb photographs and diagrams, the book represents a treatise on the subject without rival. It is a complete guide to the pathology, diagnosis, current treatment and prevention of trichinosis. Diagnostic methods are reviewed dispassionately and the varied symptomatology is thoroughly discussed.

Reference is made more than once to the fact that both the discovery of the causative organism and the recognition of the eosinophilia which usually accompanies the disease were made by undergraduate medical students James Paget in England and Thomas Brown at Johns Hopkins. Rarely are the names of Virchow and Zenker associated with this disease but their contributions to the knowledge of it were very important. This book may be recommended without reservation.

ARTHUR J. WALKER, M. D.

A Manual of Surgical Anatomy: By Tom Jones and W. C. Shepard. Philadelphia and London, W. B. Saunders Company, 1945. Pp. 195. Price $5.00.

This unique manual should prove of great value to members of the Medical Corps of the Armed Forces confronted with war surgery, which, unlike elective surgery, deals with bizarre wounds affecting all parts of the human body in rather unorthodox manner.

Although the predecessor of this volume, published in 1918 — late in the course of World War I — was an excellent, concise anatomical atlas, the present issue is truly a manual of surgical anatomy with practical emphasis on surgical considerations.

The excellent portrayals of various body regions are represented from the view in which the surgeon is likely to see tissues and organs through standard and most scientific or anatomic incisions.

The 267 splendid diagrammatic illustrations in pen and ink with color, in excellent perspective, although unaccompanied by text, speak for themselves. They will afford the user a speedy, yet adequate recollection of forgotten points of anatomy and guide him in planning the most anatomic approaches and in exercising regard for optimum conservation of tissue and preservation of function.

This manual of surgical anatomy will be of value not only to the young or even the experienced war surgeons for their necessarily hasty precursory review, but likewise will be welcomed by civilian physicians and prove to be an excellent guide in the more formal and more leisurely courses in surgical anatomy in medical schools.

This work is indeed a valuable contribution to the war effort by two very accomplished artists, Messrs. Tom Jones and W. C. Shepard, their publishers, and the members of the Committee on Surgery of the National Research Council's Medical Science Division.

HANS-KARL STAUSS, M. D.

Yellow Magic: The Story of Penicillin: By J. D. Ratcliff. Random House, New York, 1945. Pp. 173. Price $2.00.

This story of the discovery, isolation, large-scale production and clinical application of penicillin is told in the manner of a novel. The tale of the part played by each investigator is told in a very dramatic and personal manner colored by the imagined emotions of the worker. The work is somewhat marred by constant use of "staphs" and "streps", apparently intended to be plurals of the abbreviations staph. and strep., and by gratuitous bits of medical misinformation such as: a description of one organism (*B. brevis*) secreting a substance to cause shrivelling of a pneumococcus in a stained smear, the finding of staphylococcus "colonies" in a blood smear, and attributing clubbed fingers in subacute bacterial endocarditis to embolism. These are apparently due to desire to attain a dramatic effect even at the expense of accuracy. With the exceptions of such extraneous details the work is a fair history of the development of the drug. As a book intended for the layman it has no more medical errors than the average of such works and is a good book of this class.

FOSTER N. MARTIN, JR., M. D.

Arthritis and Allied Conditions: By Bernard I. Comroe, A. B., M. D., F. A. C. P. 3d ed. enl. Philadelphia, Lea & Febiger, 1944. Pp. 1359. Price $12.00.

The third edition of this standard text by Bernard I. Comroe, Chief of the Arthritis Clinic at the Hospital of the University of Pennsylvania, is bigger and better than ever. No other volume approaches it in completeness and excellence. It is more profusely illustrated than ever and thirteen new chapters have been added to cover such subjects as penicillin, psychogenic factors in rheumatic diseases, rheumatic manifestations in tropical diseases, the effect of climate on arthritis, and so on. The sections on treatment with gold and sulfonamides have been rewritten. In a sense it is almost a textbook on medical orthopedics since it contains chapters on traumatic arthritis, the painful shoulder, Dupuytren's contracture, painful feet, backache, sciatica, tumors of joints and tendon sheaths. Physical and surgical therapy are discussed in detail. The chapter on radiology, both diagnostic and therapeutic, is well illustrated.

The book is thus of interest to the specialist as well as to the general practitioner. Of particular value to the latter are chapters on the diagnostic digest of the average arthritic problem and on the differential diagnosis of rheumatoid arthritis. Since the book is a very large one, box summaries have been liberally sprinkled throughout the text which serve as compendiums of essential and practical information. Detailed instructions regarding treatment in its various forms are clear and specific. The soundly conservative views of the author are particularly valuable. This book is thus far the definitive work on the baffling problem of rheumatic diseases.

THOMAS FINDLEY, M. D.

PUBLICATIONS RECEIVED

Froben Press, New York, New York: A Surgeon Looks at Life, by Richard A. Leonardo, M. D., Ch. M., F. I. C. S.

Harvard University Press, Cambridge, Massachusetts: What People Are, by Clark W. Heath.

Lea & Febiger, Philadelphia, Pa.: Neuro-Anatomy, by Albert Kuntz, M. D., Ph. D. The Autonomic Nervous System, by Albert Kuntz, M. D., Ph. D. Essentials of Neuro-Psychiatry, by David M. Olkon, S. B., A. M., M. D. Electrotherapy and Light Therapy, by Richard Kovacs, M. D.

C. V. Mosby Company, St. Louis, Missouri: Facial and Body Prosthesis, by Carl Dame Clarke.

W. B. Saunders Company, Philadelphia, Pa.: Pathology of Tropical Diseases, by J. E. Ash, Colonel, M. C., U. S. A., and Sophie Spitz, M. D., C. S., A. U. S. A Manual of Surgical Anatomy, by Tom Jones and W. C. Shepard. A Textbook of Surgery, by Frederick Christopher, B. S., M. D., F. A. C. S.